

ASHP Guidelines on Adverse Drug Reaction Monitoring and Reporting

Am J Health-Syst Pharm. 2022;79:e83-89

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Keywords: adverse drug event, adverse drug reaction, pharmacists, surveillance, trigger medication, trigger tool

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<https://doi.org/10.1093/ajhp/zxab324>

Purpose

Pharmacists have the knowledge and expertise needed to develop and organize comprehensive programs that monitor, report, and evaluate adverse drug reactions (ADRs) in health systems. ADR monitoring and reporting programs (hereinafter, “ADR programs”) encourage surveillance, facilitate documentation, promote reporting, provide mechanisms for monitoring the safety of drug use, and stimulate the education of healthcare professionals.

The purpose of this document is to provide updated guidance for organizations initiating an ADR program or seeking to improve an existing program. The following topics are covered: common definitions, recommended program features, program goals, and the pharmacist's role in the development

of a comprehensive program. The recommendations in these guidelines represent a consensus of documented evidence, expert opinion, and professional judgment. They are written to establish reasonable goals that are progressive and challenging yet attainable as best practices in applicable settings. Pharmacy professionals are encouraged to exercise their professional judgment in assessing and adapting these recommendations to meet the specific needs of their healthcare organizations.

Definitions

The relationship between medication errors, adverse drug events, and adverse drug reactions is described in [Figure 1](#). Standardized use of these terms and definitions is recommended in order to focus attention on efforts needed to address ADRs.

Adverse drug event (ADE): harm resulting from medical intervention involving a drug.¹⁻⁴

- Adverse drug events may be preventable (ie, medication errors) or nonpreventable (ie, adverse drug reactions).
- All ADEs are associated with harm.

Harm: impairment of the physical, emotional, or psychological function or structure of the body and pain or injury resulting therefrom.³

Adverse drug reaction (ADR): a nonpreventable adverse drug event occurring with usual use of medication.^{2,3,5,6}

- ADRs are not associated with medication errors.
- Multiple organizations have defined ADRs; the above definition is a simplified version derived from these multiple sources in an effort to standardize and simplify.^{2,3,5}
- *Side effect* is a popular term typically used to describe ADRs that are known to occur with a medication with varying degrees of associated harm.
- Drug withdrawal, drug-abuse syndromes, accidental poisoning, and

drug-overdose complications should not be defined as ADRs.

Allergic ADR: an ADR that results from an immunologic hypersensitivity.

Idiosyncratic ADR: an ADR that is peculiar to the individual.

Trigger tool: Chart review, via automated or manual processes, to detect “triggers” that may be representative of an ADE or ADR.⁷ The trigger is investigated to determine whether an ADE occurred (eg, if an INR of >7 is the trigger, the chart is then reviewed to determine if warfarin is the cause).

Trigger medications: Medications commonly used to treat ADRs, such as antidotes, reversal agents, steroids, or antihistamines.⁷ Administration of a trigger medication does not always indicate that patient harm occurred.

High-alert medications: drugs that bear a heightened risk of causing significant patient harm when they are used in error.⁸

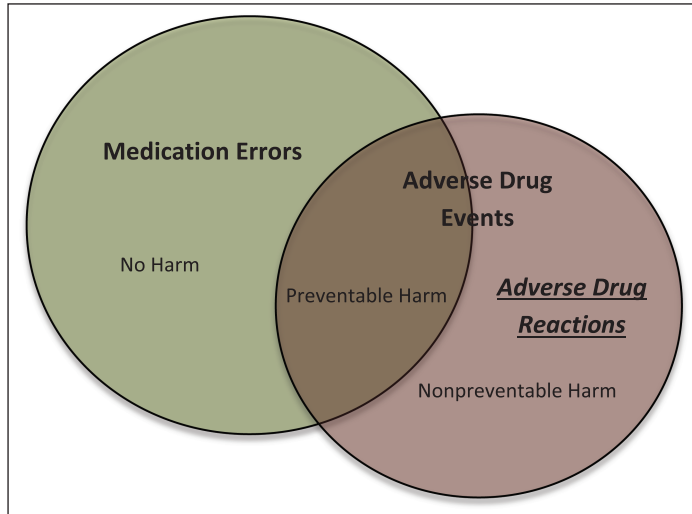
Natural language processing: computer software analysis of text contained in the electronic health record (EHR).⁹

Goals of an ADR program

The primary goal of an ADR program should be to raise awareness of the risks associated with ADRs, identify ADRs that have occurred, and reduce their risk of associated harm. An ongoing ADR program can provide benefits to the organization, patients, pharmacists, and other healthcare professionals, including (but not limited to) the following:

1. Improving patient care and decreasing length of stay by ensuring safer use of drugs and appropriate follow-up.
2. Educating healthcare professionals and patients about drug effects and increasing their level of awareness regarding ADRs.

Figure 1. Relationship between medication errors and adverse drug events. Adapted from reference 3 and from Morimoto T, Gandhi TK, Seger AC, et al. Adverse drug events and medication errors: detection and classification methods. *Qual Saf Health Care* 2004;13:306-314.



3. Providing an indirect measure of the quality of drug therapy through identification of potential ADRs and anticipatory surveillance for high-risk drugs or high-risk patients.
4. Complementing organizational risk-management activities and efforts to minimize liability.
5. Assessing the safety of drug therapies.
6. Providing quality-assurance screening to identify opportunities for medication-use evaluation or other performance improvement initiatives.
7. Characterizing ADR incidence. (ASHP does not suggest that there is a predictable rate of incidence or severity of ADRs. The number and severity of ADRs in a given organization or setting would vary with the organization's size, type, patient mix, drugs used, modalities utilized to assess risk and patient harm, the ADR definition used, and ease of reporting.)

ADR program features

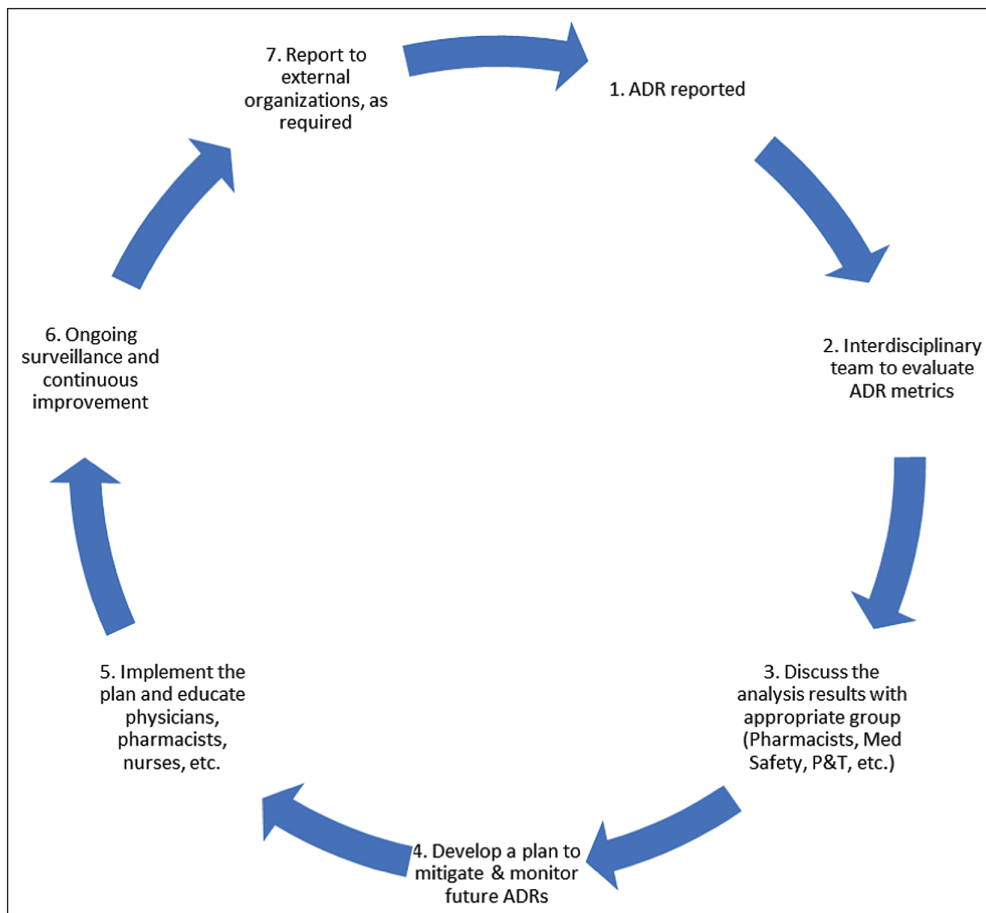
A comprehensive ADR program should be an integral part of an organization's overall drug-use system and should include the following features (Figure 2):

1. A surveillance system that spans the course of the medication-use process, including:

- a. A prospective surveillance system for high-risk drugs or patients at high risk for ADRs, which includes ongoing review of the medical literature, proactive communication to practitioners to increase awareness, and mitigation of potential harm.
- b. An ongoing and concurrent (during drug therapy) surveillance system based on the reporting of suspected ADRs by pharmacists, physicians, nurses, other caregivers, and patients.¹⁰
- c. A retrospective surveillance system to identify ADRs. This surveillance would include identifying orders for the use of trigger medications that are used to treat common ADRs (eg, orders for immediate doses of antihistamines, epinephrine, or corticosteroids), abrupt discontinuation or decreases in dosage of a drug, patient clinical assessment, or stat orders for laboratory assessment of therapeutic drug levels.¹¹⁻¹³
- d. Tools such as event monitoring, clinical decision support, and natural language processing can be used to detect certain types of ADRs in clinical databases.^{14,15}

2. Date of onset, a description of each suspected ADR, reaction type, and the outcomes from the event should be accurately documented in the patient's medical record. Some EHRs do not readily distinguish between an allergy and significant ADR without additional investigation into the record by the clinician.^{14,15} ADR monitoring and reporting programs should ensure timely and appropriate information is provided to clinicians.
3. Healthcare professionals, patients, or patient representatives should be notified following institutional policy and procedures regarding suspected ADRs.
4. Information regarding suspected ADRs should be reported to the pharmacy department 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 patient outcomes.¹⁰
5. High-risk patients should be identified and monitored.
 - a. High-risk patients include but are not limited to pediatric patients, geriatric patients, patients with organ failure (eg, hepatic or renal failure), and patients receiving antineoplastics.¹¹
6. High-risk drugs should be identified based on prescribing patterns and institutional utilization, and their use should be routinely monitored because they can also be a source of ADRs. Examples of drugs that may be considered as high-risk include but are not limited to aminoglycosides, amphotericin, antineoplastics, corticosteroids, digoxin, anticoagulants, insulin, lidocaine, phenytoin, thrombolytic agents, and opioids.^{8,11}
7. 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 ADR, the results of dechallenge and rechallenge (if any), alternative etiologies, and a literature review.
8. A method for assigning the probability of a reported or suspected ADR should be developed to categorize each ADR.

Figure 2. Features and process of a comprehensive adverse drug reaction (ADR) monitoring and reporting program. Med Safety indicates Medication Safety Committee (or similar organization); P&T, Pharmacy and therapeutics committee (or similar organization).



Many algorithms to assist in assessment of the cause of the ADR have been developed. Commonly used algorithms include the Naranjo algorithm, the WHO causality tool, and the Liverpool ADR causality tool; however, there are many others that pharmacists may find useful.^{5,16-23} 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 (ie, 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. Was there a rechallenge (ie, did symptoms return when the drug was readministered)?
9. A method for ranking ADRs by severity should be established. A commonly used scale ranks severity into 7 categories according to clinical consequence, including resultant harm and intensity of medical intervention required.²⁴ The National Cancer Institute Common Terminology Criteria for Adverse Events is a standardized system to quantify or grade the severity of adverse medication reactions.²⁵ The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) also provides a classification that can assist in coding ADEs; it considers factors such as whether an error reached the patient and whether the patient was harmed and to what degree.²⁶ The NCC MERP classification index included in the document was developed to categorize harm for medication errors. Despite being designed for medication errors, many commercial and governmental reporting programs have adopted the NCC MERP Index and applied it to all event types, including ADRs.
 10. Serious or unexpected ADRs should be reported to a medication manufacturer

and/or the FDA in accordance with state reporting requirements (Figure 2).

- a. Sequester as much evidence and clinical information as possible prior to reporting.
 - b. FDA offers 2 reporting tools, MedWatch²⁷ and the Vaccine Adverse Event Reporting System (VAERS),²⁸ which should be used to report events and allow for tracking of national safety signals.
11. ADR reports should be reviewed and evaluated by a designated interdisciplinary committee (eg, medication safety committee, pharmacy and therapeutics committee).
- a. In settings where it is possible, a pharmacy-coordinated ADR team or committee, consisting of but not limited to a physician, nurse, quality improvement leader, an administrator, a pharmacist, and an informaticist (preferably a pharmacy informaticist) is recommended.²⁹⁻³¹
 - b. The interdisciplinary committee 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.
12. ADR report information and trending should be disseminated to healthcare professional staff members for educational purposes, while maintaining confidentiality. Suggested topics for medical staff education include recognition of ADRs and appropriate and effective care for patients who experience ADRs. Educational programs can be provided in various formats, such as competencies, morning report/safety huddle discussions, newsletters, grand rounds presentations, algorithms for treatment, and interdisciplinary reviews of medication-use evaluations.
13. Findings from an ADR program should be incorporated into the organization's
- ongoing quality improvement activities. The process should include the following actions:
- a. Case-specific feedback to all appropriate healthcare staff, patients, and caregivers.
 - b. Continuous monitoring for trends, clusters, or significant individual ADRs, both internally and externally (eg, manufacturers, state boards, FDA, Institute for Safe Medication Practices).
 - i. Internal data can be trended by patient demographics (eg, gender and age), patient care area, involved drug(s) and drug class, reaction type, and severity level. Data can be reported via descriptive analysis or as a trend (Figures 3-5 provide examples). This information should be used by the interdisciplinary committee to decide further action, training, or system improvement, as appropriate. The FDA Adverse Event Reporting System (FAERS) can be utilized for trending external data through its public dashboard.³²
 - c. Educational efforts to interdisciplinary team for detection, prevention, and reporting of ADRs.
 - d. Evaluation of prescribing patterns, patient monitoring practices, patient outcomes, and the ADR program's effect on overall and individual patient outcomes.
14. Technology allowing sharing of ADR information, standardization and simplification of reporting, and automated access to external reporting databases such as MedWatch and VAERS is not widely available. Adoption of these features should be considered by the ADR program as they become available.

Role of the pharmacist in ADR monitoring and reporting

Pharmacists are a vital link between the patient and the health system before and during the course of drug

therapy.^{33,34} Pharmacists are uniquely qualified to provide valuable information on drug products, can play an important role in monitoring adverse events, and help design and implement system improvements related to ADRs in their health systems.^{35,36}

Pharmacists should obtain formal endorsement or approval of such programs through appropriate committees (eg, a pharmacy and therapeutics committee and the executive committee of the medical staff) and the organization's administration. In applicable settings, input into the design of the program should be obtained from the medical staff, nursing staff, quality improvement staff, the medical records department, and risk managers.^{19,37-39}

The pharmacist should facilitate the following activities:

1. Analysis of each reported ADR.
2. Identification of drugs and patients at high risk for being involved in ADRs.
3. The development of scope, 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 routine evaluation of ADR records within the organization, including the use of standardized reporting rate and incidence of onsite ADRs occurrence.
7. The organizational dissemination and use of information obtained through the ADR program.
8. Facilitating the reporting of serious or unexpected ADRs, as outlined in program features section 2, and publication and presentation of important ADRs to the medical community.

Conclusion

Pharmacists are uniquely positioned to assist in the coordination of an ADR program. Programs should focus on surveillance, complete documentation within medical records,

Figure 3. Adverse drug reaction (ADR) trending by involved drug using Pareto principle. In the example, Drug A was the top reported medication involved in ADR events, a trend that can be used as a signal to warrant additional investigation.

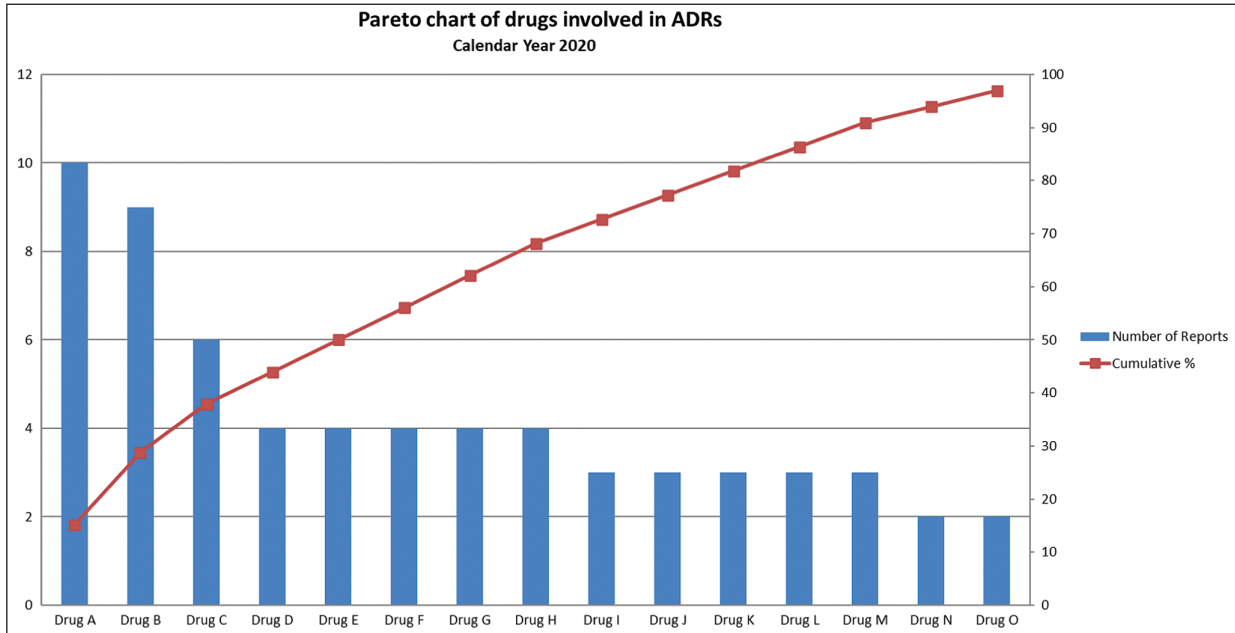
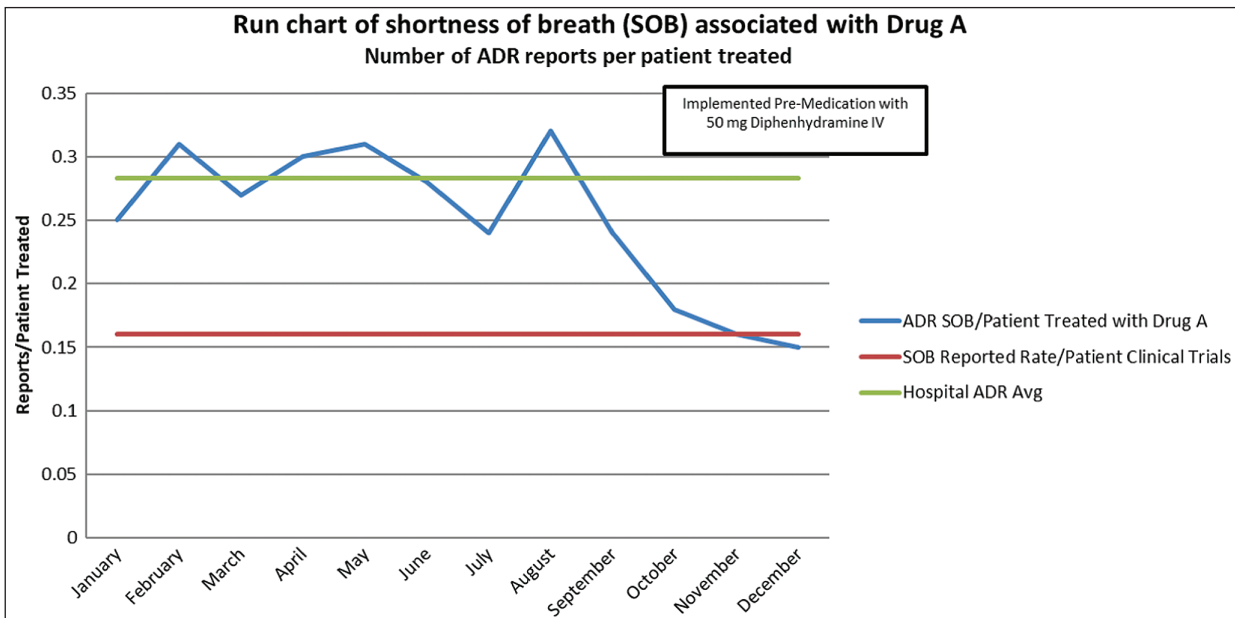


Figure 4. Example of monthly adverse drug reaction (ADR) event trending of the top reported medication identified in Figure 3. In the example, shortness of breath (SOB) ADR events involving Drug A were captured on a monthly basis and the event rate compared with the hospital’s ADR average (green line) and reported SOB events resulting from the use of Drug A in clinical trials (red line). Based on the trends noted, an intervention was made in August to premedicate patients, and this milestone is depicted on the graph.

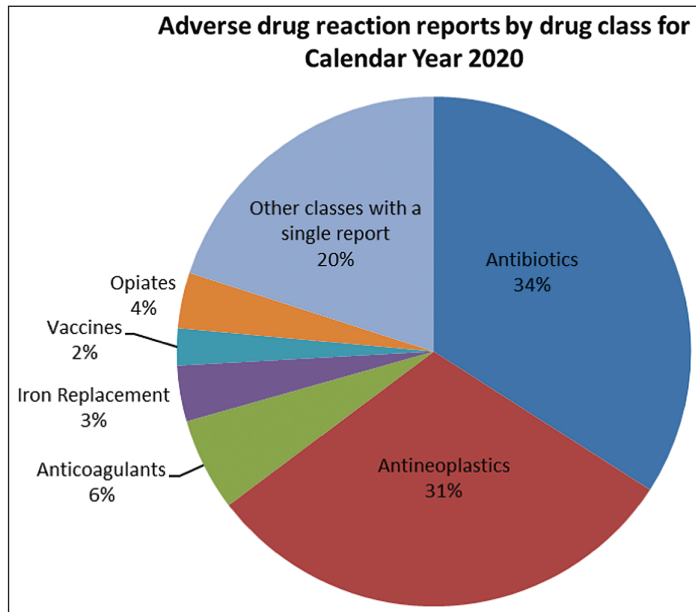


reporting to and review by an interdisciplinary committee, and education to achieve an overall goal of

reducing the risk and severity of ADRs within an organization. All pharmacists should understand their role in

recognizing, evaluating, reporting, and educating both patients and providers on ADRs.

Figure 5. Example of organization of data on reported adverse drug reaction events by involved drug class in a pie chart.



Acknowledgments

ASHP gratefully acknowledges the following organizations and individuals for reviewing these guidelines (review does not imply endorsement): American Association of Critical-Care Nurses (AACN); Institute for Healthcare Improvement (IHI); Institute for Safe Medication Practices (ISMP); Maryland Society of Health-System Pharmacy (MSHP); Sandra Leigh Bardas, BSPharm, RPh, FCSHP; James L. Besier, PhD, MS, BSPharm, FASHP; Carol J. Bickford, PhD, RN-BC, CPHIMS, FAMIA, FHMSS, FAAN; John Bowman, MS, BCPS, FASHP; Jamie N. Brown, PharmD, BCPS, BCACP; Kavish Choudhary, PharmD, MS; Michael R. Cohen, RPh, MS, ScD (hon), DPS (hon), FASHP (ISMP); Michael C. Dejos, PharmD, BCPS, LSSBB, DPLA; Frank Federico, RPh (IHI); Katayoon Kathy Ghomeshi, PharmD, MBA, BCPS, CPPS; Jennifer Howard, PharmD; Anna Hu, PharmD; Melissa Jones, PhD (AACN); Thomas Kaye, RPh, MBA, FASHP; Nicole Kiehle, PharmD, BCPS (MSHP); Eric C. Kutscher, PharmD, MBA, FASHP; Mark A. Malesker, PharmD, FCCP, FCCP, FCCM, FASHP, BCPS; Patrick M. Malone, PharmD, FASHP; Linda Gore Martin, PharmD, MBA, FASHP; Robert B. McDaniel, PharmD, BCPS; Charles D. Ponte, BPharm, PharmD, FAADE, FAPhA, FASHP, FCCP, FNAP; James Ponto, MS, FASHP; Robert L. Poole, PharmD, FPPAG, FCSHP, FASHP; James R. Rinehart, RPh, MS, FASHP; Richard I. Sakai, PharmD, FASHP, FCSHP; Adam Servi, PharmD, RPh, BCPS; Karen W. Smollen, PharmD; Kristin

A. Tuiskula, PharmD; GERALYN Waters, PharmD, BCPS; and Debbie Wu, PharmD. ASHP also gratefully acknowledges the contributions of authors of previous versions of these guidelines: Philip E. Johnston, PharmD, Charles P. Coe, BSPharm, and Karen E. Koch, PharmD.

Disclosures

The authors have declared no potential conflicts of interest.

Additional information

Developed through the ASHP Section of Inpatient Care Practitioners and approved by the ASHP Board of Directors on May 20, 2021. These guidelines supersede the ASHP Guidelines on Adverse Drug Reaction Monitoring and Reporting dated November 16, 1994.

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