

at public workshops and forums (e.g., sponsored by the Drug Information Association (DIA) or the Pharmaceutical Education and Research Institute (PERI)). The agency has considered these comments in development of this proposed rule.

Once this proposed rule is finalized, the agency will provide the public with an overview of the provisions in the rule at workshops and forums (e.g., DIA meetings, PERI workshops). All firms, including small firms, would have an opportunity to attend these presentations.

Firms can access AERS-related information on the Internet at <http://www.fda.gov/cder/aers/index.htm>. The AERS site includes a "Reporting Regulations and Guidances" page that provides a summary of the rulemaking (proposed rules, final rules) and guidances regarding the agency's safety reporting requirements for human drugs and biological products. This site is updated as changes to the safety reporting requirements are made.

V.F. Unfunded Mandates Reform Act of 1995

On the basis of the preceding discussion, under the Unfunded Mandates Reform Act, FDA concludes that if only .85 percent of the estimated SADR are prevented, then the benefits of this proposed rule will exceed the annualized compliance costs that it imposes on the U.S. economy. In addition, the agency has considered other alternatives as discussed in section V.E.4 of this document and determined that the proposed rule is the best alternative that would meet the objectives of this rule.

V.G. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Friedman, Michael A. *et al.*, "The Safety of Newly Approved Medicines: Do Recent Market Removals Mean There Is a Problem?" *Journal of the American Medical Association*, 281:1728–1734, 1999.
2. Murphy, Barbara M., and Lawrence C. Frigo, "Development, Implementation, and Results of a Successful Multidisciplinary Adverse Drug Reaction Reporting Program in a University Teaching Hospital," *Hospital Pharmacy*, 28:1199–1204, 1993.
3. Beyth, Rebecca J., and Ron Shorr, "Epidemiology of Adverse Drug Reactions in the Elderly by Drug Class," *Drugs & Aging*, 14:231–239, 1999.
4. Cooper, James W., "Adverse Drug Reaction-Related Hospitalizations of Nursing Facility Patients: A 4-Year Study,"

Southern Medical Journal, 92:485–490, 1999.

5. Gaines, Ann R., and Frederick Varricchio, "Interferon Beta-1b Injection Site Reactions and Necroses," *Multiple Sclerosis*, 4:70–73, 1998.
6. Schumock, Glen T. *et al.*, "Control Charts to Monitor Rates of Adverse Drug Reactions," *Hospital Pharmacy*, 30:1088–1096, 1995.
7. Johnston, Philip E., Jason D. Morrow, and R. A. Branch, "Use of a Database Computer Program to Identify Trends in Reporting of Adverse Drug Reactions," *American Journal of Hospital Pharmacy*, 47:1321–1327, 1990.
8. Kennedy, Diane L. *et al.*, "National Adverse Drug Event Reporting," *American Journal of Hospital Pharmacy*, 50:1913–1914, 1993.
9. Pierce, L. Ross *et al.*, "Hemolysis and Renal Failure Associated With the Use of Sterile Water for Injection to Dilute 25% Human Albumin Solution," *American Journal of Health Systems Pharmacy*, 55:1057–1070, 1998.
10. Institute of Medicine, edited by Linda T. Kohn *et al.*, "To Err is Human: Building a Safer Health System," National Academy Press, 1999.
11. Tyler, Linda S., and Nancy A. Nickman, "Hospital Pharmacy Compliance with JCAHO Standards and ASHP Guidelines for Reporting Adverse Drug Reactions," *American Journal of Hospital Pharmacy*, 49:845–850, 1992.
12. U.S. Department of Health and Human Services, Office of the Inspector General, "Review of the Food and Drug Administration's Handling of Adverse Drug Reaction Reports," Report No. A–15–98–50001, 1999.
13. Einarson, Thomas R., "Drug-Related Hospital Admissions," *The Annals of Pharmacotherapy*, 27:832–840, 1993.
14. U.S. Department of Commerce, "Statistical Abstract of the United States," 1999.
15. Agency for Health Care Policy and Research, "National Medical Expenditure Survey: Annual Expenses and Sources of Payment for Health Care Services Research Findings 14," p. 7, 1995.
16. Bates, David W. *et al.*, "The Costs of Adverse Drug Events in Hospitalized Patients," *Journal of the American Medical Association*, 277:307–311, 1997.
17. The U.S. General Accounting Office, "Adverse Drug Events The Magnitude of Health Risk Is Uncertain Because of Limited Incidence Data," GAO/HEHS–00–21, January, 2000.
18. Lazarou, Jason *et al.*, "Incidence of Adverse Drug Reactions in Hospitalized Patients, A Meta-Analysis of Prospective Studies," *Journal of the American Medical Association*, 279:1200–1205, 1998.
19. Classen, David C. *et al.*, "Adverse Drug Events in Hospitalized Patients Excess Length of Stay, Extra Costs and Attributable Mortality," *Journal of the American Medical Association*, 277:301–306, 1997.
20. Thomas, Eric J. *et al.*, "Costs of Medical Injuries in Utah and Colorado," *Inquiry*, 36:255–264.

21. Ives, Timothy J. *et al.*, "Drug-Related Admissions to a Family Medicine Inpatient Service," *Archives of Internal Medicine*, 147: 1117–1120, 1987.

22. McKinney, James M., and W. L. Harrison, "Drug-Related Hospital Admissions," *American Journal of Hospital Pharmacy*, 33:792–795, 1976.

23. Caranasos, George J. *et al.*, "Drug-Induced Illness Leading to Hospitalization," *Journal of the American Medical Association*, 228:713–717, 1974.

24. Johnson, Jeffrey A., and J. Lyle Bootman, "Drug-Related Morbidity and Mortality, A Cost of Illness Model," *Archives of Internal Medicine*, 155:1949–1956, 1995.

25. Eastern Research Group, Inc., "Cost of Implementing MedDRA Terminology for Pharmaceutical and Biologics Companies," 2000.

26. Goodnough, Lawrence T. *et al.*, "Transfusion Medicine," *The New England Journal of Medicine*, 340:438–447, 1999.

27. Newman, B.H., "Donor Reactions and Injuries From Whole Blood Donation," *Transfusion Medicine Reviews*, 11:64–75, 1997.

28. "International Reporting of Periodic Drug Safety Update Summaries," Final Report of the CIOMS Working Group II, 1992.

29. "Current Challenges in Pharmacovigilance: Pragmatic Approaches," Final Report of the CIOMS Working Group V, 2001.

VI. Paperwork Reduction Act of 1995

This proposed rule contains collections of information which are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public obtain, maintain, retain, or report information to the agency, or disclose information to a third party or to the public. The title, description, and respondent description of the information collection are shown below with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, gathering and maintaining the data needed, and completing and reviewing the collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information