

- d. Changes to CCSI
- e. Worldwide patient exposure
- f. Individual case safety reports
- i. Line listings
- ii. Summary tabulations
- g. Safety studies
- h. Other information
- i. Overall safety evaluation
- j. Conclusion
- k. Appendices
 - i. Company core data sheet
 - ii. U.S. labeling
 - iii. Spontaneous reports submitted to the applicant by an individual other than a health care professional
 - iv. SADR with unknown outcome
 - v. Class action lawsuits
 - vi. Lack of efficacy reports
 - vii. Information on resistance to antimicrobial drug products
 - viii. Medication errors
 - ix. U.S. patient exposure
 - x. Location of safety records
 - xi. Contact person
- 3. Interim Periodic Safety Reports (IPSRs)
- 4. Semiannual Submission of Individual Case Safety Reports
- 5. Reporting Requirements
 - a. Reporting intervals
 - b. Submission date
 - c. Cover letter
 - d. International birth date for combination products
- F. Reporting Format
 - 1. Forms Versus Narrative Format
 - 2. Medical Dictionary for Regulatory Activities (MedDRA)
 - 3. Single Form for Each Identifiable Patient
 - 4. Contact Person
 - 5. Computer-Generated Facsimile of FDA Form 3500A or Vaccine Adverse Event Reporting System (VAERS) Form
 - 6. Other Revisions
- G. Patient Privacy
- H. Recordkeeping
- I. Abbreviated New Drug Application (ANDA) Products
 - J. Postmarketing Approved New Drug Application (NDA) and Biologics License Application (BLA) Annual Reports
- K. Safety Reporting for In Vivo Bioavailability and Bioequivalence Studies
 - L. Proposed Implementation Scheme
- IV. Environmental Impact
- V. Analysis of Impacts
 - A. Background and Summary
 - B. Market Failure
 - C. Benefits
 - 1. Expanded Safety Information
 - 2. Improved Uniformity and Quality of Safety Information
 - 3. Potential Savings from Reduced SADR-Related Hospitalizations
 - a. Reduced rate of SADR-related hospitalizations
 - b. Reduced rate of in-hospital SADR
 - c. Indirect benefits of reducing the hospital costs of SADR
 - d. Sum of SADR-related costs
 - 4. Cost Savings and More Efficient Use of Resources
 - a. Savings related to maintaining and building data bases of SADR and intercompany transfers of drug safety data
 - b. Savings related to greater ease in entering into intercompany agreements
 - c. Savings related to eventual international harmonization to the PSUR format
 - d. Potential savings in clinical trial management
 - e. Leveraging specialized knowledge
 - f. Total benefits
 - D. Costs of Compliance
 - 1. Costs of New Recordkeeping and Reporting Requirements
 - a. Number of reports
 - b. New time burden
 - i. Expedited reports
 - ii. Followup reports
 - iii. Blood products
 - iv. IND and bioavailability/bioequivalence safety reports
 - v. Semiannual submissions of postmarketing individual case safety reports
 - vi. Postmarketing period safety reports (TPSR, PSUR, and IPSR)
 - vii. Other reports
 - c. Annual cost of the reporting and recordkeeping provisions
 - 2. Costs of MedDRA
 - a. One-time costs
 - i. Planning and coordination
 - ii. Development of information technology support structure
 - iii. Purchase or development of an autoencoder
 - iv. Conversion of legacy safety data
 - v. Training of personnel
 - vi. Revision of standard operating procedures (SOPs)
 - b. Recurring costs
 - i. MedDRA core subscription
 - ii. MedDRA versions and quarterly updates
 - iii. Maintenance of existing dictionaries
 - E. Small Business Analysis
 - 1. Need for and Objectives of the Rule
 - 2. Description and Estimate of Small Entities
 - 3. Projected Reporting, Recordkeeping, and Other Compliance Requirements
 - a. Reporting and recordkeeping requirements
 - b. Implementing MedDRA
 - 4. Alternatives and Steps to Minimize the Impact on Small Entities
 - a. Do nothing
 - b. Do not require a medical dictionary
 - c. Do not require medication errors as expedited reports
 - d. Do not require blood establishments to submit reports for all serious SADR associated with blood collection and transfusion
 - e. Do not require certain bioavailability and bioequivalence reports as expedited reports
 - f. Waivers for economic hardship
 - g. Small business outreach, training, and assistance
 - F. Unfunded Mandates Reform Act of 1995
 - G. References
- VI. Paperwork Reduction Act of 1995
 - A. Expedited Safety Reporting
 - B. Periodic Safety Reports
 - C. Other Reports
 - D. Recordkeeping
- VII. Executive Order 13132: Federalism

I. Previous Safety Reporting Rulemaking and Current Guidances

FDA has undertaken a major effort to clarify and revise its regulations regarding pre- and postmarketing safety reporting for human drug and biological products. Since 1990, several rules and guidances have been issued regarding these regulations. Some of these guidances have been issued by international organizations (*i.e.*, ICH and CIOMS), while others have been issued by FDA. In figure 1 of this document, FDA illustrates how these rules and guidances relate to the current proposed rule.

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