

percent, the annual benefit will exceed \$10 million. Thus, while it has been determined that the final rule is significant under the Executive order, the final rule will not be economically significant as defined by the Executive order, because the annual impacts on the economy are substantially below

\$100 million. With respect to the Regulatory Flexibility Act, the agency certifies that this final rule will not have a significant effect on a substantial number of small entities. The effect of small entities is discussed in more detail in section V.D of this document. The Unfunded Mandates Reform Act

does not require FDA to prepare a statement of costs and benefits for the final rule because the rule will not result in any 1-year expenditure that would exceed \$100 million adjusted for inflation. The current inflation-adjusted statutory threshold is about \$110 million.

TABLE 1.—SUMMARY OF QUANTIFIABLE BENEFITS AND COSTS (\$MILLION)

Benefits and Costs	One-Time	Annual	Total
Benefits¹			
Avoided cost of hospital infections		3.8	3.8
Indirect cost of longer hospital stays		0.4	0.4
Indirect costs of mortality (discounted at 3% and 7%)		6.6–11.8	6.6–11.8
Total Benefits		10.8–16.0	10.8–16.0
Costs²			
One-time labeling revision	2.9		0.42
Annual incremental printing cost		0.02	0.02
Annual Physicians Desk Reference (PDR)		0.123	0.123
Costs			
Total Costs	2.9	0.146	0.568

¹ Assumes medical, productivity, and mortality costs now attributable to antibacterial resistance are reduced by 1 percent.

² May not sum to total because of rounding.

A. Objective of the Final Rule

Drug-resistant bacteria pose a public health risk by reducing the effectiveness of prescription antibacterial drug products. Some disease-producing bacteria can adapt and become resistant to newly developed drugs within a couple of years. For example, a report of infections resistant to linezolid, the first drug in a new class of antibiotics, was published just 1 year after its approval (Ref. 6). To stress the need for continued vigilance against the emergence of resistant bacteria, the final rule requires that labeling of systemic antibacterial drug products include statements that encourage the use of antibiotics in a way that reduces the risk of developing drug-resistant bacteria. The final rule requires that labeling for affected prescription drug products comply with the requirements by February 6, 2004.

B. Costs of Regulation

The agency received several comments about the costs of the proposed rule. One comment asked whether the economic analysis in the proposed rule included the cost of initial and followup doctor visits or the cost of culture and sensitivity tests. Because patients normally see a health care provider to obtain a prescription for an antibacterial drug, the agency's initial analysis of impacts did not include costs for health care visits.

The agency also did not estimate the number or cost of laboratory tests that might have been ordered because of the proposed labeling change. Many doctors

and hospitals currently order susceptibility tests, especially when there is a high incidence of resistant bacterial infections locally. In any event, in response to comments, the agency has revised the wording of the proposed statement that suggested a general need for susceptibility testing. Instead, the final rule adds statements to antibacterial labeling that remind health care providers to consider laboratory results, if available, when selecting drug therapy. Because the final rule does not require additional laboratory tests or visits to health care providers, this analysis of impacts does not include these patient health care costs as regulatory costs.

Some comments questioned the cost-effectiveness of susceptibility testing. The agency did not evaluate the cost-effectiveness of laboratory tests. As stated elsewhere in the preamble, the agency has modified the language about susceptibility tests to clarify that initial drug therapy should be modified if available test results suggest the infection is caused by different microorganisms than initially suspected, not by testing each patient.

One comment stated that waiting to initiate drug therapy would lead to additional health care, morbidity, and mortality costs. While the agency agrees that any delay in starting therapy can increase the direct and indirect costs of infection, the final rule does not suggest that health care providers postpone treatment once they strongly suspect that an infection is caused by a bacteria.

The agency agrees that costs increase when resistant bacteria are not initially identified as the cause of an infection. In one study on bloodstream infections, the length of hospital stay increased by 6.4 days and mortality increased from 11.9 percent to 29.9 percent with inadequate treatment (defined as either giving an incorrect drug for an infection-causing pathogen or giving the correct drug for an infection-causing pathogen that is resistant to the drug) (Ref. 7). The objective of the final rule is to reduce the prevalence of and costs associated with resistant bacteria and their associated costs. A more detailed discussion of avoided costs follows in section V.C of this document.

1. Affected Products

The final rule will affect all systemic antibacterial drug products except those primarily indicated to treat a mycobacterial infection. Antifungal, antiviral, antiparasitic, and topical antibacterial products will not be subject to the labeling requirements of the final rule. FDA estimates that manufacturers will be required to modify labeling of 669 antibacterial drug products.²

² Derived from FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations*, 2002, and 2001 Drug Information, American Hospital Formulary Service (AHFS). Products counted and active ingredients matching the AHFS lists of antibacterial agents, and a distinct manufacturer, active ingredient, or dosage form. Topical dosage forms were excluded. Products with different

Continued