

TABLE 5.—ESTIMATED NUMBER AND MONETARY VALUE OF LIFE-YEARS LOST FROM DEATHS DUE TO INFECTIONS WITH DRUG-RESISTANT BACTERIA¹

Age cohort	Average Life Years Remaining for Each Cohort ²	Number of In-Hospital Diagnoses With Drug-Resistant Infections ^{3, 4}	Number of Deaths From Drug-Resistant Infections ⁵	Number of Life Years Lost From Drug-Resistant Infections	Monetary Value of Life Years Lost—3% Discount Rate (\$ Mil) ^{6, 7}	Monetary Value of Life Years Lost—7% Discount Rate (\$ Mil) ^{6, 8}
Birth–17	69.2	3,056	0.3	21.2	\$4.4	\$7.8
18–44	48.1	10,372	1.3	62.0	\$12.7	\$22.8
45–64	26.8	16,807	11.8	317.1	\$65.2	\$116.8
65–84	12.3	39,857	165.2	2,039.5	\$419.1	\$751.3
85+	4.2	13,838	178.4	750.6	\$154.2	\$276.5
Total		83,930	357.0	3,190.3	\$655.6	\$1,175.3

¹ Numbers may not sum or multiply due to rounding.

² Anderson, R. N., "United States Life Tables, 1997," *National Vital Statistics Reports*, vol. 47, Table 1, 1999.

³ 1997 hospital discharge data from HCUPnet, Healthcare Cost and Utilization Project, "AHRQ, Rockville, MD (<http://www.ahrq.gov/data/hcup/hcupnet.htm>).

⁴ Includes all reported ICD-9 V09 diagnoses (i.e., infection with drug-resistant microorganisms).

⁵ Baseline mortality from table 4 of this document. The number of deaths from drug-resistant infections was derived from published reports and HCUP data. Drug resistance increased mortality rates across all age cohorts by a weighted average of 27.1 percent. The mean percent increase in mortality rates and the estimated share of infections caused by the bacteria (shown in parentheses) are: 88 percent (5.3 percent) for vancomycin resistant *Enterococci* (Refs. 24, 25, 26, 27, 28, 29, 30, 31, 32, and 33); 103 percent (7.4 percent) for methicillin resistant *S. aureus* (Refs. 9, 10, 27, and 35); and 230 percent (6.5 percent) for *P. aeruginosa* (Refs. 12 and 36). No difference in mortality rates between resistant and susceptible strains was assumed for all other infection-causing bacteria. $27.1 \text{ percent} = (0.053 \times 0.88) + (0.074 \times 1.03) + (0.065 \times 2.30) + (0.808 \times 0)$ (may not sum or multiply to total because of rounding).

⁶ \$5 million = value of statistical life saved; 34.9 years = median age of population in 1997; 44.3 years remaining from 1997 Life Table, used to amortize \$5 million (see footnote 2 of this table).

⁷ \$205,493/life-year lost.

⁸ \$368,404/life-year lost.

3. Reduced Direct and Indirect Costs

Many factors can contribute to the development of antibiotic resistance, including the unnecessary use of antibiotics. The final rule adds statements to the professional labeling of these drugs that will encourage health care providers and patients to use antibiotics in a way that reduces the risk that antibiotic-resistant bacteria will develop, thus maintaining the effectiveness of these drugs.

As discussed elsewhere in this document, some comments to the agency questioned the effectiveness of labeling as an information tool. Health care organizations and government, however, can employ a variety of ways to inform stakeholders of the serious public health threat posed by resistant bacteria. Labeling that prompts health care providers and patients to use antibacterial drugs prudently will complement the educational efforts of organizations such as the AMA and CDC. The agency finds that while many health care providers infrequently consult the actual package insert, they often refer to the PDR for information about available drugs. Both the print and electronic versions of the PDR reproduce the professional labeling verbatim. Moreover, many patients use the PDR to obtain information about the drugs they are taking.

FDA cannot accurately quantify the magnitude of the impact that these changes in labeling will have on physician and patient behavior, or of its

subsequent impact on the development of resistant bacteria and their societal costs. If, however, the changes avoid even 1 percent of the above estimated costs of antibacterial resistance, the annual cost savings will amount to \$3.8 million in direct hospital costs, \$0.4 million in lost productivity, and from \$6.6 million to \$11.8 million in life-years lost (discounted at 3 percent and 7 percent respectively), for a total benefit exceeding \$10 to \$16 million annually.

If the costs of increased antibiotic resistance were decreased as little as 0.01 percent, the benefits of this rule would exceed the compliance costs estimated in the previous paragraph. FDA believes it is extremely likely that the decrease in the excess cost of antibiotic resistance will be at least this large, and is likely to be significantly larger.

D. Impacts on Small Entities

No comments on the initial regulatory flexibility analysis were received by the agency. The final rule affects manufacturers of systemic antibacterial drug products. The 1997 Economic Census found approximately 700 pharmaceutical preparation manufacturing firms in the United States (i.e., North American Industry Classification System (NAICS) code 325412). The Small Business Administration (SBA) considers firms with fewer than 750 employees to be small. As seen in table 6 of this document, Census data classify firms in

size categories that do not permit a precise determination of the number of pharmaceutical firms that have fewer than 750 employees. However, Census data do show that more than 90 percent of pharmaceutical manufacturers have fewer than 500 employees, and thus are small businesses (Ref. 12).

Approximately 101 large and small firms manufacture systemic antibacterial drug products¹⁰ and thus would be affected by the rule. The estimated annualized costs of \$861 per product¹¹ are relatively modest for most manufacturers of antibiotic drugs. Since small manufacturers of human prescription drugs already submit labeling to FDA, the labeling requirements of the rule will not require small firms to seek employees with additional special skills. As physicians and patients become more cautious in their use of antibiotics, some small antibiotic manufacturers could experience a decline in the demand for their products. The objective of the final rule is to safeguard the effectiveness of all antibiotic drug products. Thus, slowing the appearance of more resistant strains of bacteria will increase the demand for those antibiotic drugs that remain an effective treatment for those infections. More prudent use of

¹⁰ Derived from FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations*, 2001, and *2001 Drug Information*, American Hospital Formulary Service.

¹¹ Total annualized costs per product: \$417,056 + \$24,439 + \$134,720 = \$576,216. Average annualized costs: \$576,216/669 = \$861.