per preventable ADE is $532. Bar code systems are expected to avoid 12.8 ADEs per year in an average hospital. This implies an average reduction in annual legal awards of $6,800 per hospital and $43.9 million for all hospitals. Fewer awards would also result in lower malpractice insurance premiums, which would reduce other hospital expenditures. The General Accounting Office (GAO, 1995) reported hospital malpractice insurance rates ranging between $511 and $7,734 per bed, depending on location. Recent reports have suggested that annual premiums have increased to approximately $1,250 to $18,800 per bed. Although we were unable to quantify average hospital malpractice premiums or precise reductions in hospital liability insurance premiums due to the use of bar codes, the potential exists for industry savings. While reductions in legal settlements or liability insurance premiums represent transfers between hospitals, third-party payers, attorneys, and patients, and are not opportunity gains or losses, such reductions could increase the efficient allocation of resources by sector.

Bar code systems may also increase hospital revenues by improving the "cost capture rate." One published study (Lee et al., 1992) reported the cost capture rate (the ratio of billed uncontrolled pharmaceuticals to all pharmaceuticals used) increased from 63 percent to 97 percent after installation of computerized systems in nursing wards. According to the authors, this would imply an increase in revenues of approximately $65,000 per year for an average hospital. While such accounting improvements are transfers from patients and third-party payers to hospitals rather than reduced opportunity costs, this practice illustrates the potential use of bar code scanning systems in increasing the efficient allocation of resources by sector.

Other potential transfers may include avoidance of certain billing errors or increased timeliness of payment.

M. Comparison of Costs, Expenditures, and Benefits

The annualized costs of the proposed rule to the manufacturing, packaging, and labeling sectors totals $3.2 million. Hospitals would incur an annualized cost of $0.6 million to continue current operating practices. FDA resource costs to support the regulation equal an estimated $1.3 million per year. Thus, we estimate the annualized regulatory cost of the proposed rule to be $5.1 million. In addition, we expect the proposed rule to spur earlier investment by hospitals in bedside point-of-care systems that read bar coded labels. The annualized opportunity cost of this accelerated investment in technology is $680.0 million for the entire industry. Table 6 presents, by sector, the present value of the estimated regulatory costs, the annual costs expected at the end of the 20-year evaluation period, and the annualized costs over the entire evaluation period. The estimated reduction in hospital operating expenses results from the assumption that hospitals could eliminate in-house labeling operations.

TABLE 6.—COSTS AND OTHER EXPECTED EXPENDITURES OF PROPOSED RULE (IN MILLIONS OF DOLLARS; 20-YEAR EVALUATION PERIOD; 7-PERCENT DISCOUNT RATE)

Industry Sector	Present Value of Costs	Annual Operating Costs at End of Period	Annualized Costs
Prescription Drugs	$30.4	$0.4	$2.9
OTC Drugs	[1]	$2.1	$0.2
Blood Products	[1]	$0.7	$0.1
Sub-Total Manufacturers	$33.2	$0.5	$3.2
Hospital Regulatory	$6.1	(-$0.7)[2]	$0.6
Sub-Total Private Sector Regulatory Costs	$39.8	(-$0.2)	$3.8
FDA Oversight	$13 8	$1.3	$1.3
Total Regulatory Costs	$53.1	$1.1	$5.1
Expected Expenditures From health care Sector	$7,204.3	(-$348.8)[2]	$680.0

[1] Less than $0.05 million
[2] Hospital operating costs decrease due to fewer in-house packaging and bar coding operations.

As discussed above, we estimate the annualized public health benefit to be $3.9 billion. This estimate includes the societal value of the avoided ADEs as well as the reduced hospital stays expected due to the earlier use of bar

code reading technology. Other indirect potential benefits, such as efficient inventory control, patient tracking, electronic generation of daily reconciliation and medication reports, or other administrative gains were estimated to contribute an annualized amount of between $451.5 and $721.5 million in efficiency gains to hospitals. The likely distributional effects of revenue enhancement, other cost capture measures, or reduced legal costs are not completely quantified, but are likely.

If all costs and expenditures are combined, the annualized outlays total $685.1 million. The expected annualized public health benefit of over $3.9 billion far outweighs these outlays. Thus, the annual net benefits for the entire evaluation period are greater than $3.2 billion. Moreover, this calculation does not account for the potential efficiency gains as described above.

N. Uncertainty and Sensitivity

We recognize that the expected impacts of the proposed rule are based on a large number of uncertain assumptions. We attempted to account for this uncertainty by examining the key assumptions in the analysis.

1. Voluntary Share of Labeling Costs

The costs attributable to the proposed rule are the incremental costs above what the industry would incur in the normal course of business. As briefly discussed earlier, many drug products change labels, on average, as often as once a year for marketing or design reasons. The ERG estimate, however, assumes that 30 percent of the required labeling costs would be attributable to the regulation, due to the production process changes that would be required to use bar coding equipment. In addition, we believe that market driven label changes are not completely comparable to regulation required changes. We reviewed the sensitivity of this assumption by examining the impact that

would occur if no required re-labeling costs were attributable to the regulation, 75 percent were attributable to the regulation, or all re-labeling costs were attributable to the regulation. These scenarios altered the current estimate of $3.2 million in annualized costs for manufacturers, repackers, and relabelers to a range of from $2.7 million (if all costs are considered voluntary) to $4.2 million (if no additional labeling costs are considered voluntary).

2. Packaging Decisions

We are sensitive to industry packaging decisions and asked our contractor to specifically assess the impact of the proposal on the future of unit-dose packaging (e.g. blister packs) trends. The concern was whether bar code printing would reduce the use of unit-dose packaging because it would add more to its cost than to other formats. In general, ERG found that although the overall demand for the product is inelastic, the demand for a particular package type is more elastic in that it is affected by relative prices to a greater degree. Industry contacts, however, noted that this impact is moderated because consumers of some OTC drug product are accustomed to blister packs, and manufacturers could lose market share if they abandon this format. Also, many hospitals require drug purchases to be in unit-dose form.

ERG concluded that although a bar code requirement would increase the relative cost of the unit-dose version of a product, the cost increment would not be great enough to significantly impact the market. In fact, ERG found that the expected reduction in hospital over-packaging could increase market demand for unit-dose products despite the cost difference. Thus, we expect that the proposed rule would not have a significant impact on product packaging choices.

3. Mortality Associated with ADEs

FDA's contractor estimated that 2.8 percent of preventable ADEs are fatal. This was derived by averaging results from several medical studies. These studies relied on relatively small samples and varying methodologies. Due to the uncertainty attached to this estimate and the major impact this assumption has on valuing public health benefits, we tested two additional mortality rates: one percent and 0.1 percent. These rates reduce the expected value of an avoided ADE from $183,900 to $91,500 and $46,400, respectively, by changing the probability distribution of the expected outcomes of ADEs. The impact on the expected annualized benefits of ADE avoidance fall from $3.9 billion to $2.0 billion and $1.0 billion respectively. These estimated benefits continue to exceed the costs.

4. Value per QALY

There is no precise measure of value for quality-adjusted life-year. We have used published estimates of society's implied value of a statistical life (VSL) of $5 million derived from wage premiums required to attract employment to higher risk occupations. The life expectancy of a 35 year-old blue-collar male employee (the basis for most of the wage premium data) was adjusted for expected future bed and nonbed disability. When the implied VSL is amortized over the 41.3 years of adjusted life-expectancy, using a 7-percent discount rate, the resulting value ($373,000) may suggest a societal willingness-to-pay for a QALY. Cost-effectiveness studies in the health economics literature have often relied on lower values, such as $100,000, to represent the monetary value of a QALY. In addition, the $5 million VSL is based on research conducted in the early 1990's and relies on relative risk and relative wages.

Other typical estimates of the VSL have ranged from as low as $2 million to as high as $8 million.

We analyzed the societal benefit of the proposed rule using $100,000 as the QALY value for preventing a nonfatal ADE and the low VSL estimate of $2 million as the willingness-to-pay to avoid a fatality. The willingness-to-pay to avoid an average ADE decreased from $183,900 to $70,800 using these parameters. Overall, the estimated annualized benefit of the proposed rule fell from $3.9 billion to $1.5 billion, which would still exceed the estimated annualized costs.

5. Hospital Response Rates

The expected benefits rely on a faster rate of hospital acceptance of bar code technology than the rate expected in the absence of the regulation. The current estimate of public health benefits is based on all hospitals acquiring bar coding systems within 10 years as compared to 20 years without the proposed rule. However, because we are not requiring hospitals to make this investment, we examined the impact of different diffusion rates. ERG examined two additional scenarios: one in which the technology is accepted within 20 years with a rule as compared to 30 years without a rule, and one in which technology is accepted within 15 years, as compared to 20 years with a rule. Both cases decrease costs and benefits. The first case reduced expected net annualized net benefits from $3.2 billion to $2.0 billion. Annualized hospital expenditures declined from $680 million to $408 million, and benefits decreased from $3.9 billion to $1.8 billion. The second case reduced annualized net benefits to $1.5 billion. Annualized hospital expenditures declined from $680 million to $303 million, and benefits decreased from $3.9

billion to $1.8 billion. The public health benefits of the proposed rule would still exceed costs and expenditures with these slower diffusion rates.

6. Hospital Intercept Rates with Machine-Readable Technology

The expected benefit of avoidance of patient ADEs is dependent on the expected rate of error interception. For this analysis, ERG found that about 45 percent of the errors that lead to preventable ADEs originate in the dispensing and administration stages of the medication process and that the use of bar coded information and installed systems would intercept about 50 percent of these errors. Because of the direct relationship between expected interception rates and avoided ADEs, we tested the impact of the assumed rates. Although the literature has implied that interception rates as high as 85 percent are obtainable, ERG assumed a 50 percent rate to account for potential nonoptimal use of technology. If the true increase in interception rates were between 80 percent and 20 percent, the total number of avoided ADEs would be between 660,400 and 165,000. The monetized annualized value of these avoided ADEs would vary from the current estimate of $3.9 billion to the lower and higher values of $1.6 billion (with a 20 percent improvement in interception rates) or $6.2 billion (with an 80 percent improvement in interception rates). From a societal perspective, therefore, the accelerated technology investment appears reasonable even with significantly lower interception rates.

7. Productivity Losses in Hospital Wards

The decision by hospitals to make significant investments in bar code reading technology is highly dependent on expected productivity changes in the delivery of bedside care by nurses. Our current analysis assumes a 3-percent productivity loss of ward nurses due to the use of this new technology.

We examined the sensitivity of this estimate and found that if long-term productivity loss approximated only 1 percent of the current workload, the average annualized cost of accelerated hospital investments would decrease from $680.0 million to $246.7 million. However, if the productivity loss of nursing resources was as great as 5 percent, the annualized expenditures by hospitals would increase to $1.2 billion. In order for the productivity losses to outweigh the expected benefits, however, there would have to be an almost 700-percent estimated productivity loss. We recognize the extreme uncertainty of this projection and particularly invite public comment in this area.

8. Investments by Hospital Size

The internal decision to acquire and use new bar code reading technology could be affected by the size of the purchasing hospital. Hospitals that have already installed this equipment are, for the most part, fairly large or part of a large network of hospitals. Because the benefits of error interception are dependent on the number of annual admissions, we were concerned about the likelihood of technology adoption by small hospitals.

According to the most recent census, there are 1,117 hospitals in the United States with capacities fewer than 50 beds. These hospitals account for only about 3 percent of the estimated annualized opportunity cost of investment from this proposed rule, because the potential productivity losses are not as great as for larger hospitals. The annualized opportunity costs per facility with fewer than 50 beds is approximately $57,100. However, because of the fewer admissions to hospitals of this size, we estimate that the interception rate of the bar code technology is expected to result in an average of 1.7 avoided ADEs per year per facility. The estimated societal benefit of avoiding 1.7 ADEs is $303,800. If these small hospitals adopt technology at

the same accelerated rate as all hospitals, the annualized benefit per hospital is $86,900, or more than the investment.

We are aware that the estimated direct annual hospital cost savings of avoiding ADEs alone ($2,257 per avoided ADE) may not cover the costs of the expected earlier investment pattern. For example, the average facility with fewer than 50 beds would experience direct annual cost savings of $3,837 (1.7 ADEs avoided x $2,257) and annualized costs of $57,100. As noted, the investment decision to install bar code reading technology is voluntary and would include consideration of patient safety and other cost-savings. We have estimated that potential reductions in resources needed to generate reports and to keep track of records may likely vary between $27,400 and $43,700 per year for a small hospital. Other institutional gains, including transfers such as increased revenue capture rates and reduced malpractice awards, may also affect internal decisions. Many industry representatives have indicated their willingness to invest in this technology. Nonetheless, even if some hospitals choose to delay or not to invest, this rule would still produce substantial societal benefits.

O. Small Business Analysis and Discussion of Alternatives

We believe the proposed rule is unlikely have a significant impact on a substantial number of small entities. Despite this, we have prepared an initial Regulatory Flexibility Analysis (IRFA) and invite comment from affected entities. In addition, the regulation is considered a significant economic impact under UMRA and alternatives are examined and briefly discussed here.

1. Affected Sectors and Nature of Impacts

We described the affected industry sectors earlier in this section. The proposal would directly affect manufacturers of pharmaceutical and biological

products (NAICS 325412 and NAICS 325414), packaging services (NAICS 561910), and blood and organ banks (NAICS 621991), and indirectly affect hospitals (NAICS 622). We accessed data on these industries from the 1997 Economic Censuses and estimated revenues per establishment. Although other economic measures, such as profitability, may be preferable alternatives to revenues in estimating the significance of regulatory impacts in some cases, any reasonable estimate of profits would not change the results of this analysis. These revenues were updated to 2000 values by using the Consumer or Producer Price Index as appropriate.

a. *Pharmaceutical Manufacturers (NAICS 325412).* The Small Business Administration (SBA) has defined as small any entity in this industry with fewer than 750 employees. According to census data, 84 percent of the industry is considered small. The average annual revenue for these small entities is $26.6 million per entity. Small manufacturers of prescription and OTC drug products dispensed under an order and commonly used in hospitals would be required to generate and label products with bar coded information. We estimate the annualized compliance costs for small entities in this industry at $1,800 per entity. This is less than 0.1 percent of their annual revenues. We believe this does not constitute a significant impact on a substantial number of small entities in this industry.

b. *Biological Product Manufacturers (NAICS 325414).* The SBA has defined as small any entity in this industry with fewer than 500 employees. According to census data, 68 percent of the industry is considered small. The average annual revenue for these small entities is $4.7 million per entity. Small manufacturers of biological products would be required to use standardized bar code information on their products. We estimate the annualized

compliance costs for small entities in this industry at $600 per entity. This is less than 0.1 percent of their annual revenues. We believe this does not constitute a significant impact on a substantial number of small entities in this industry.

c. *Packagers (NAICS 5619190).* The SBA has defined as small any entity in this industry that has less than $6 million in annual revenues. On this basis, almost 75 percent of the industry is considered small. The average annual revenue for small entities is $1.7 million per entity. Small packagers would be required to apply bar coded information to all affected products. This would require printing and process improvements to packaging operations. We estimated the annualized compliance cost for small entities in this industry at $240 per entity. This is less than 0.1 percent of their annual revenues. We believe this does not constitute a significant impact on a substantial number of small entities in this industry.

d. *Blood and Organ Banks (NAICS 621991).* The SBA has defined as small any entity in this industry with less that $8.5 million in annual revenues. On this basis, 40 percent of the industry is considered small. The average annual revenue for small entities is $1.4 million per entity. Small blood banks and collection centers would be required to apply standardized bar coded information on all blood products. This would require printing and process improvements to blood handling operations. We estimated the annual compliance cost for small entities in this industry at $100 per entity. This is less than 0.1 percent of their annual revenues. We believe this does not constitute a significant impact on a substantial number of small entities in this industry.

e. *Hospitals (NAICS 622).* The SBA has defined as small any entity in this industry with less than $29.0 million in annual revenues. According to census data, 35 percent of the industry is considered small. The average annual revenue for small entities is $12.6 million per entity. There is no specific regulatory requirement for hospitals to respond to this proposed rule. We anticipate that the rule would make the investment in bar code technology more attractive to hospitals, but the rule would not require such investments. Hospitals that have already installed bar code reading systems and internally affix self-generated information might need to prematurely upgrade or replace currently installed scanners in order to capture bar coded information on small vials or bottles. These hospitals would also achieve productivity gains by avoiding the resources now used to self-generate bar code readable information. The total annual net cost of the proposed rule is estimated at $3,300 per facility, which is equal to less than 0.1 percent of annual revenues. We believe this does not constitute a significant impact on a substantial number of small entities in this industry.

2. Alternatives

We considered several alternatives to the proposed rule. Each is discussed below. We invite comments and suggestions for additional potential alternatives.

a. *Do Nothing.* This alternative would not result in any change in current labeling or packaging practices. We believe that, in the absence of agency action, hospitals would gradually purchase and utilize independent bar code reading systems, but that it would take 20 years before they were installed in all facilities. We rejected this alternative because of the expected positive net benefits of the proposal. Also, we believe that standardizing bar codes

would generate additional health and production efficiencies for a variety of different health care sectors.

b. *Requiring Variable Information.* We considered requiring additional information in bar codes, such as expiration dates and lot numbers. The incremental benefit of this data would include improved inventory control and ease of recalls. In addition, we are aware that some firms are voluntarily applying this information. However, we were unable to quantify potential public health benefits for this additional information, and the estimated additional annualized cost of this alternative was $46.0 million. We did not select this alternative because we could not demonstrate that the added benefits would exceed the added costs.

c. *Covering All OTC Drug Products.* We considered requiring all OTC drug products to include bar coded information. This alternative is currently rejected (although we invite comments on the OTC drugs to be covered) because the additional costs do not appear to be justified by the expected benefits. At this time, most noninstitutional settings are unlikely to have access to bar code reading systems. Therefore, we could not identify any significant reductions in ADEs due to this alternative. Including all OTC drug products would create estimated additional annualized costs to the manufacturing sector of $1.9 million. The expected annualized costs of the regulation therefore would increase from $5.1 million to $7.0 million with no additional quantifiable benefit.

d. *Exemption for Small Entities.* We considered exempting small entities, but rejected the alternative due to the modest projected impact of this initiative on small businesses and the lack of label standardization that would result.

e. *FDA Selecting a Specific Symbology.* We considered requiring bar coded information with a specific symbology. The rationale for considering this option was to minimize uncertainty to hospitals in selecting systems that would be able to confidently read the specific language. We decided, however, that identifying a specific symbology might adversely impact future innovations in other machine-readable technologies. The selected alternative would allow individual facilities and suppliers to devise systems that would maximize their own internal efficiencies, as long as the standardized information could be accessed. The lack of consistent universal standards has been a major impediment to the use of this technology. As long as symbologies could be read within a single standard, however, the identified market failure would be overcome. In addition, the expected costs of this proposal would be much greater than the selected alternative. Annualized costs to manufacturers would increase to $8.3 million and significant costs would occur to the retail sector due to the need for accelerated upgrade or replacement of currently installed scanners. Retail pharmacies would incur annualized costs of $14.4 million. Consequently, we rejected the alternative of identifying a specific symbology.

3. Outreach

We held a public meeting on July 26, 2002 to solicit comments from the affected sectors. Interested parties from the health care sector, manufacturing sector, retail sector, and equipment suppliers provided comment and insight to the agency. In addition, we met with various industry groups in order to ensure viewpoints were appropriately considered. These insights affected the regulatory considerations, and additional outreach is planned during the regulatory process.

P. Conclusion

We have examined the proposed rule and find that the expected benefits outweigh the costs and that the regulation would improve public health. The detailed analysis that provides references and support for the summary that appears in this section is available in the docket as Ref. 46.

VIII. Request for Comments

In addition to requesting general comments on the proposal, and the specific requests on assumptions contained in the economic analysis, we are seeking comment on the following specific issues identified in the description of the proposed rule (presented here for the convenience of the reader):

1. Whether we should require bar codes on prescription drug samples, and the costs and benefits associated with such bar codes (see section II.B.2.a of this document).

2. The risks and benefits of including vaccines in a bar code rule (see section II.B.2.a of this document).

3. What terms we should use to describe OTC drugs that should be subject to the bar code requirement (see section II.B.2.b of this document).

4. Information on the costs and benefits associated with putting lot number and expiration date information in the bar code (see section II.C.2 of this document).

5. Whether the rule should refer instead to linear bar codes without mentioning any particular standard or refer to UCC/EAN and HIBCC standards (see section II.D.1 of this document).

6. Additional information regarding bar code scanning technology and the ability of bar code scanners to read different symbologies (see section II.D.1 of this document).

7. Whether the rule should adopt a different format (whether that format is a symbology, standard, or other technology), considering the following issues:

• What other symbol, standard, or technology should we consider, either in place of a linear bar code or in addition to it?

• How accepted is that symbol, standard, or technology among firms that would have to affix or use that symbol, standard, or technology?

• Will hospitals be able to read or use the symbol, standard, or technology, either with existing equipment or equipment under development? (see section II.D.1 of this document).

8. Whether any specific product or class of products should be exempt from a bar code requirement and the reasons why an exemption is considered to be necessary (see part II, section F). In addition, how could we create a waiver provision that would minimize the potential for misusing the waiver?

9. Whether we should require the use of ISBT 128 for blood products, a specific symbology that is consistent with that required for drugs in proposed § 201.25, or "machine-readable symbols" as approved by the Director of CBER (see section II.H of this document).

10. How the proposed rule might affect hospitals where patients receive blood or blood components, particularly with respect to a hospital's decision to purchase a machine reader (e.g., scanner) that can properly identify the intended recipient of the blood or blood component, the machine readable information encoded on the blood or blood component label, and perhaps the linear bar codes appearing on drugs and OTC drugs that are dispensed pursuant to an order and commonly used in the hospital (see section II.H of this document).

11. Whether any of the alternatives discussed in the economic analysis have merit.

Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments to http://www.fda.gov/dockets/ecomments or two hard copies of any written comments, except that individuals may submit one hard copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

IX. References

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

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8. Testimony of Tommy G. Thompson, Secretary of Health and Human Services, before the Senate Committee on Health, Education, Labor, and Pensions' Subcommittee on Patient Health, May 24, 2001.

9. Letter from Henri R. Manasse, Jr., Executive Vice President and Chief Executive Officer, ASHP, to the Honorable Tommy G. Thompson, Secretary of Health and Human Services, dated July 10, 2001, at p. 1.

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Quality Interagency Coordination Task Force (QuIC) to the President," at page 74 (February 2000).

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44. FDA, "Guidance for Industry: Recognition and Use of a Standard for the Uniform Labeling of Blood and Blood Components," June 2000, at page 1.

45. Food and Drug Administration, "Guidance for Industry: United States Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128," November 1999, at section 1, page 2.

46. Eastern Research Group, "Impact of Proposed Barcode Regulations for Drug and Biological Products," Contract Number 223–98–8002, Task Order Number 21, December 2, 2002.

47. Eastern Research Group, "Profile of Machine-Readable Technologies for Medical Applications," Contract Number 223–94–8031, In partial fulfillment of Task Order Number 8, December 2, 2002.

Appendix

Additional Information on Various Studies Identifying Different Types of Medication Errors

This appendix includes summaries of several articles that identify different types of medication errors, a table illustrating varied medication error rates among studies, and a list of references cited in the appendix.

I. Types of Medication Errors Administering the Wrong Dose

Folli et al. examined errant chart orders in two large pediatric hospitals (Ref. A–1). The study defined an errant chart order as a potentially lethal error if certain consequences (such as cardiopulmonary arrest if administered at the dose ordered) resulted. The authors found that incorrect doses and missed doses were the most prevalent errors. Overdoses accounted for 55 percent of the dosing errors, while underdoses led to 26.9 percent of all errors.

In a study of adverse events in hospitalized patients, Leape et al. reviewed 30,195 randomly selected hospital records and identified 1,133 patients whose disabling injuries were caused by medical treatment (Ref. A–2). Errors in dose or method of use accounted for 42 percent of all errors.

In a study of two urban teaching hospitals, Kaushal et al. found dosing errors to be the most frequent medication error (which the authors defined as errors in drug ordering, transcribing, dispensing, administering, or monitoring) and the most frequent preventable adverse drug event (Ref. A–3).

Lesar et al. conducted a study of prescribing errors at a teaching hospital (Ref. A–4). The authors' review of 289,411 medication orders revealed 905 prescribing errors that were detected and averted, and overdoses and underdoses accounted for 28.7 and 17.8 percent of total errors respectively.

McCarthy, Kelly, and Reed studied the medication administration practices of school nurses (Ref. A–5). The authors found that 48.5 percent of school nurses surveyed reported medication errors, and overdoses or double doses were the third most commonly reported error (22.9 percent of medication errors).

Administering a Drug to a Patient Who Is Known to Be Allergic

In the Lesar review of medication orders, 6.7 percent of all medication order errors that were detected and averted involved prescribing a drug to a patient who is allergic to the prescribed drug (Ref. A–4).

In an article by Classen et al. involving a case control study of all patients admitted to a hospital in a 3-year period, medication errors due to known drug allergies represented 1.5 percent of all adverse drug events, and all were preventable (Ref. A–6).

Administering the Wrong Drug to a Patient or Administering a Drug to the Wrong Patient

A study by Thur et al. observed how nurses in two surgical units prepared to administer parenteral admixtures (which the authors defined as including only fluids to which one or more drugs were added directly into a single or primary bottle) (Ref. A–7). The authors defined "medication error" as including the administration of the wrong drug or solution, the wrong dosage of a drug or solution volume, an unordered or discontinued drug, or two or more pharmaceutically incompatible drugs in the same admixture. The study

involved 100 observations where 331 parenteral admixtures were prepared; unordered drugs accounted for 3 percent of the errors that were observed. In one instance, the drug was administered two times per day for 4 days, even though the order for the drug had been discontinued earlier.

In the Classen et al. article that involved a case control study, of 905 prescribing errors that were detected and averted, 1.1 percent of all errors involved prescribing a drug to the wrong patient (Ref. A–6).

Administering the Drug Incorrectly

In the study by Kaushal et al. that examined 10,778 medication orders at two urban teaching hospitals, errors involving the drug's route of administration were the second most common form of medication error and accounted for 18 percent of the medication errors (Ref. A–3). These medication errors also accounted for the third-most common form (14 percent) of potential adverse drug events, which the authors defined as a medication error having a significant potential for injuring a patient.

Administering the Drug at the Wrong Time or Missing Doses

In a study of two pediatric critical care units by Tisdale, "wrong time" errors, which were defined as medications administered 30 minutes before or after the scheduled administration time, were the most prevalent error and accounted for a 16 percent error rate (Ref. A–8).

In McCarthy, Kelly, and Reed's study of school nurses, of the 315 school nurses who reported a medication error, 251 cited missed doses as the most common medication error (Ref. A–5).

In their study of the relationship between medication errors and adverse drug events, Bates, Boyle, et al. found that 53 percent of the medication errors surveyed involved at least one missing dose of medication (Ref. A–9).

A recently published study by Barker et al. examined 36 institutions in Colorado and Georgia and found that 19 percent of the doses administered were in error and that the most prevalent error (at 8 percent of the medication errors) was "wrong time" medication errors (Ref. A–10). The authors defined "wrong time" as administration of a dose more than 60 minutes before or after the scheduled administration time, or a 30 minute window for medications that were ordered before, with, or after a meal. However, the "wrong time" medication error rate ranged between zero percent for some nonaccredited hospitals in Georgia to 26.2 percent for a nonaccredited hospital in Colorado.

II. Frequency of Medication Errors

Table 1 illustrates the variation in medication error rates among several studies. Some studies suggest a medication error rate of under 7 percent, whereas others suggest a rate at or above 20 percent. The differences may be due, in part, to different definitions of medication error or different research methodology that focused on fatalities, injuries, or medication orders.

TABLE 1.—MEDICATION ERROR RATES REPORTED IN VARIOUS STUDIES

Study	Definition of Medication Error Used	Medication Error Rate
Observation of nurses in two surgical units by Thur (Ref. A–7).	"Medication error" defined as wrong drug or solution; wrong dosage of a drug or solution volume; an unordered or discontinued drug; or two or more pharmaceutically incompatible drugs in the same admixture.	21%
Review of 101,022 medication orders at 2 pediatric hospitals by Folli et al. (Ref. A–1).	"Errant medication order" considered to be an order that was not in accordance with standard pediatric references, current published literature, or dosing guidelines approved by the hospital's pharmacy and therapeutics committees.	Medication order error rate was between 4.9 and 4.5 errors per 1,000 orders.
Review of 289,411 medication orders written during a 1-year period by Lesar (Ref. A–4).	Not defined.	Prescribing errors were detected at a rate of 3.13 errors per 1,000 orders.
Survey of 26,462 patients in 7 countries; 24 were considered to have died as a result of a drug or group of drugs by Porter and Jick (Ref. A–11).	"Suspected adverse reactions" defined as any undesired or unintended effect of a drug.	0.02% fatality rate (6 deaths were considered preventable).
Review of 30,195 randomly selected hospital records by Leape et al. (Ref. A–2).	"Adverse event" defined as an unintended injury caused by medical management and resulted in measurable disability. The reviewers considered an adverse event to be due to "negligence" if they felt there was a deviation from accepted norms of treatment and after they considered other factors (such as potential consequences, frequency of risk, degree of emergency, and complexity of the case). The authors defined "negligence" as failure to meet the standard of care reasonably expected of an average physician qualified to take care of the patient in question.	Of the adverse events due to drug treatment, 18% resulted from negligence, although the authors also explain that negligence occurs not merely when there is error, but when the degree of error exceeds an accepted norm.
Study of 18,262 medication and intravenous fluid orders given in a 3–month period at a children's hospital by West et al. (Ref. A–12).	Not defined.	Medication order error rate ranged between 2.6 to 8.5 per 1,000 orders. Verbal medication orders had the lowest error rate, followed by computer-entered orders (6.3 per 1,000) and handwritten orders.

TABLE 1.—MEDICATION ERROR RATES REPORTED IN VARIOUS STUDIES—Continued

Study	Definition of Medication Error Used	Medication Error Rate
Study of 4,031 adult admissions of 11 medical and surgical units in 2 hospitals by Bates, Cullen et al. (Ref. A–13).	"Adverse drug event" defined as an injury resulting from medical intervention related to a drug.	28% of adverse drug events are preventable, and there were 7.3 preventable adverse drug events per every 100 admissions.
Review of 10,070 medication orders to identify medication errors by Bates, Boyle et al. (Ref. A–9).	"Medication error" defined as errors in the process of ordering or delivering medication, regardless of whether an injury occurred or the potential for injury was present.	5.3%.
Matched case-control study of all patients admitted to a hospital in a 3-year period by Classen et al. (Ref. A–6).	"Adverse drug event" defined as an event that is "noxious and unintended and occurs at doses used in humans for prophylaxis, diagnosis, therapy, or modification of physiologic functions" but excludes therapeutic failures, poisonings, and intentional overdoses.	1% of all adverse drug events, but the authors also state that almost 50% of all adverse drug events are potentially preventable.
Review of 10,778 medication orders at 2 urban teaching hospitals by Kaushal et al. (Ref. A–3).	"Medication errors" defined as errors in drug ordering, transcribing, dispensing, administering, or monitoring.	5.7%, with adult patients cared for in a pediatric setting experiencing the most medication errors.
Prospective cohort study in 36 institutions by Barker et al. (Ref. A–10).	"Medication error" defined as a dose administered differently than as ordered on the patient's medical records.	19%, or nearly 2 errors every day for a typical patient receiving 10 doses per day, or, for a facility with 300 patients, almost 40 potential adverse drug events in a facility. The percentage of potentially harmful errors was 7% or more than 40 per day per 300 inpatients.
Examination of all U.S. death certificates between 1983 and 1993 by Phillips et al. (Ref. A–14).	Medication errors are "accidental poisonings by drugs, medicaments, and biologicals" and have resulted from "acknowledged errors, by patients or medical personnel.	"Medication error rate rose from 1 out of every 439 outpatient deaths and 1 out of every 1, 622 inpatient deaths in 1983 to 1 out of every 131 outpatient deaths and 1 out of every 854 inpatient deaths in 1993. The authors suggest the increase may be due to an increasing willingness to attribute error deaths that were previously ascribed to natural causes.

III. References in the Appendix

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

A–1. Folli, H. L., R. L. Poole, W. E. Benitz, et al., "Medication Error Prevention by Clinical Pharmacists in Two Children's Hospitals," *Pediatrics*, 79:718–722, 1987.

A–2. Leape, L. L. et al., "The Nature of Adverse Events in Hospitalized Patients," *New England Journal of Medicine*, 324:377–384, 1991.

A–3. Kaushal, R. et al., "Medication Errors and Adverse Drug Events in Pediatric Inpatients," *Journal of the American Medical Assosciation* 285:2114–2120, 2001.

A–4. Lesar, T. S. et al., "Medication Prescribing Errors in a Teaching Hospital," *Journal of the American Medical Assosciation* 263:2329–2334, 1990.

A–5. McCarthy, A. M., M. W. Kelly, and D. Reed, "Medication Administration Practices of School Nurses," *Journal of School Health*, 70:371–376, 2000.

A–6. Classen, D.C. et al., "Adverse Drug Events in Hospitalized Patients," *Journal of the American Medical Assosciation*, 277:301–306, 1997.

A–7. Thur, M. P., "Medication Errors in a Nurse-Controlled Parenteral Admixture Program," *Journal of Hospital Pharmacy*, 29:298–304, 1972.

A–8. Tisdale, J. E., "Justifying a Pediatric Critical-Care Satellite Pharmacy by Medication-Error Reporting," *American Journal of Hospital Pharmacy*, 43:368–371, 1986.

A–9. Bates, D.W., D. L. Boyle, M. B. Vander Vliet, et al., "Relationship Between Medication Errors and Adverse Drug Events," *Journal of General Internal Medicine*, 10:199–205, 1995.

A–10. Barker, K. N. et al., "Medication Errors Observed in 36 Health Care Facilities," *Archives of Internal Medicine*, 162:1897–1903, 2002.

A–11. Porter, J., and H. Jick, "Drug-Related Deaths Among Medical Inpatients," *Journal of the American Medical Assosciation*, 237:879–881, 1977.

A–12. West, D. W., S. Levine, G. Magram, et al., "Pediatric Medication Order Error Rates Related to the Mode of Order Transmission," *Archives of Pediatric and Adolescent Medicine*, 148:1322–1326, 1994.

A–13. Bates, D. W., D. J. Cullen, N. Laird, et al., "Incidence of Adverse Drug Events and Potential Adverse Drug Events," *Journal of the American Medical Assosciation* 274:29–34, 1995.

A–14. Phillips, D. P., N. Christenfeld, and L. M. Glynn, "Increase in US Medication-Error Deaths Between 1983 and 1993," *Lancet*, 351: 643–644, 1998.

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 606

Blood, Labeling, Laboratories, Reporting and recordkeeping requirements.

21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that parts 201, 606, and 610 be amended as follows:

PART 201—LABELING

1. The authority citation for 21 CFR Part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg–360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 263.

2. Section 201.25 is added to read as follows:

§ 201.25 Bar code label requirements.

(a) Who is subject to these bar code requirements? Manufacturers, repackers, relabelers, and private label distributors of a human prescription drug product or an OTC drug product that is regulated under the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act are subject to these bar code requirements unless they are exempt from the registration and drug listing requirements in section 510 of the act.

(b) What drugs are subject to these bar code requirements? The following drug products are subject to the bar code label requirements: Prescription drug products (excluding samples), biological products, and over-the-counter drug

products that are dispensed under an order and are commonly used in hospitals. For purposes of this section, an over-the-counter drug product is "commonly used in hospitals" if it is packaged for institutional use, labeled for institutional use, or marketed, promoted, or sold to hospitals.

(c) What does the bar code look like, and where does the bar code go?

(1) Each drug product described in paragraph (b) in this section must have a bar code that contains, at a minimum, the appropriate National Drug Code (NDC) number in a linear bar code that meets Uniform Code Council (UCC/EAN) standards. Additionally, the bar code must:

(i) Be surrounded by sufficient blank space so that the bar code can be scanned correctly; and

(ii) Remain intact under normal conditions of use.

(2) The bar code must appear on the drug's label as defined by section 201(k) of the act.

PART 606—CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS

3. The authority citation for part 606 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 360j, 371, 374; 42 U.S.C. 216, 262, 263a, 264.

4. Section 606.121 is amended by revising paragraph (c)(13) to read as follows:

§ 606.121 Container label.

* * * * *

(c) * * *

(13) The container label must bear encoded information that is machine-readable and approved for use by the Director, Center for Biologics Evaluation and Research.

(i) Who is subject to this machine-readable requirement? All blood establishments that manufacture, process, repackage, or relabel blood or blood components intended for transfusion and regulated under the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act.

(ii) What blood products are subject to this machine-readable requirement? All blood and blood components intended for transfusion are subject to the machine-readable information label requirement in this section.

(iii) What information must be machine-readable? Each label must have machine-readable information that contains, at a minimum:

(A) A unique facility identifier,

(B) Lot number relating to the donor,

(C) Product code, and

(D) ABO and Rh of the donor.

(iv) How must the machine-readable information appear? The machine-readable information must:

(A) Be unique to the blood or blood component;

(B) Be surrounded by sufficient blank space so that the machine-readable information can be scanned correctly; and

(C) Remain intact under normal conditions of use.

(v) Where does the machine-readable information go? The machine-readable information must appear on the label of any blood or blood component which is or can be transfused to a patient or from which the blood or blood component can be taken and transfused to a patient.

* * * * *

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

5. The authority citation for part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374; 42 U.S.C. 216, 262, 263, 263a, 264.

6. Section 610.67 is added to read as follows:

§ 610.67 Bar code label requirements.

Unless it is regulated as a device, a biological product must comply with the bar code requirements at § 201.25 of this chapter.

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[FR Doc. 03–????? Filed ??–??–03; 8:45 am]

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