DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Electronic Distribution of Prescribing Information for Human Prescriptions Drugs, Including Biological Products

Docket No. FDA- 2007-N-0363

Proposed Regulatory Impact Analysis
Proposed Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis

Economics Staff
Office of Planning
Office of Policy, Planning, and Legislation
Office of the Commissioner

Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). This proposed rule would be an economically significant regulatory action under Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. The proposed rule would have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $141 million, using the most current (2012) Implicit Price Deflator for the Gross Domestic Product. FDA expects this proposed rule to result in a 1-year expenditure that would meet or exceed this amount.

A. Summary

The proposed rule would generate costs to set up a system for the electronic distribution of prescribing information for human prescription drugs. While this system may support other or

all components of the product labeling in addition to the prescribing information, this proposed rule covers the prescribing information portion of product labeling.

The proposed rule would generate costs for users of prescribing information who would need additional hardware, training, Internet access, and information access time. In addition, incremental costs would be associated with some printing of the prescribing information. Table 1 shows a summary of the ranges of annualized costs using discount rates of 7 percent and 3 percent over 10 years. The proposed rule would generate benefits in the form of production cost savings because eliminating the production of most paper forms would reduce the costs of providing prescribing information on human prescription drugs. Table 1 shows the ranges of savings. The large ranges for both costs and savings indicate the uncertainty associated with such a large change in practices for such a large number of manufacturers and users. If we use a 7 percent discount rate to annualize the costs and savings over 10 years, the effects of the proposed rule could range from annualized net savings of $5.0 million to annualized net savings of $73.5 million. With a 3 percent discount rate to annualize cost savings, the effects could range from an annualized net savings of $10.0 million to annualized net savings of $82.2 million. These quantified effects do not include the public health benefits associated with users having access to the most up-to-date versions of the prescribing information.

Table 1.--Summary of Annualized Costs and Cost Savings (in millions)

	Low (7%)	High (7%)	Low (3%)	High (3%)
Cost Savings	$51.8	$163.7	$56.6	$170.8
Costs	$46.8	$89.2	$46.6	$88.6
Net Savings (Cost Savings – Costs)	$5.0	$73.5	$10.0	$82.2

Table 2.--Economic Data: Costs and Benefits Statement

Units							
Category	Primary Estimate	Low Estimate	High Estimate	Year Dollars	Discount Rate	Period Covered	Notes
Benefits:							
Annualized Monetized $millions/year	107.2	51.8	163.7	2010	7%	10 years	Monetary benefits are net cost savings to manufacturers and other label providers
	113.7	56.6	170.8	2010	3%	10 years	
Annualized Quantified					7%		
					3%		
Qualitative							Reduced adverse events through reduced prescribing errors due to out-of-date label information
Costs:							
Annualized Monetized $millions/year	68.0	46.8	89.2	2010	7%	10 years	Costs to users of prescribing information
	67.6	46.6	88.6	2010	3%	10 years	
Annualized Quantified					7%		
					3%		
Qualitative							
Transfers:							
Federal Annualized Monetized $millions/year					7%		
					3%		
From/To	From:			To:			
Other Annualized Monetized $millions/year					7%		
					3%		
From/To	From:			To:			
Effects:							
State, Local, or Tribal Government: No Effect							
Small Business: The proposed rule would affect small entities that use prescribing information, mainly small pharmacies and hospitals							
Wages: No effect							
Growth: No effect							

B. Need for the Rule

The proposed rule would ensure that health care professionals have access to the most current prescribing information. The Agency recognizes that the current system of requiring the paper form of prescribing information to physically accompany prescription drugs may lead to the continued dissemination of out-of-date prescribing information. The information in the prescribing information is intended for the prescriber and other health care professionals but it is

mostly the pharmacist who has ready access to it. Prescribers (physicians) have come to rely more heavily on compendiums containing the information that is compiled by third parties. Most of the compendiums do not contain the universe of drugs on the market or may not provide a complete version of the prescribing information. Often, these compendiums are in paper form such as a book. When there is a change to a product's prescribing information, which is a common occurrence, products with the older version of the prescribing information generally remain on pharmacy shelves, and there can be considerable lags in updating the information in compendiums. An electronic system of distributing the prescribing information can ensure that those accessing it have the most up-to-date version. The proposed rule would not affect the supply or use of compendia.

A single electronic labeling repository for prescribing information accessible to all users is a public good that can be provided efficiently through regulation. To ensure that health care professionals can obtain prescribing information with a minimum of search time, there needs to be a single repository containing the prescribing information for all drug products in a standard form that can be universally accessed and printed (if necessary) using existing technology. Our regulations already require all manufacturers to provide FDA with the information contained in the prescribing information electronically at the time of listing (part 207). This proposed rule would require the submission of prescribing information to FDA in an electronic format that FDA can process, review, and archive (currently SPL format) each time there is a change in the labeling, and under our enforcement authority we would be able take action when manufacturers do not provide labeling that is up to date.

We propose to phase out the current requirement for paper forms of prescribing information altogether (except for products that would be subject to the exemption provisions of

this regulation) within 2 years of publication of the final regulation to eliminate confusion as to which prescribing information should be referenced.

C. Public Health Benefits

The potential public health benefits may come from fewer prescribing errors made due to out-of-date information. These benefits cannot be quantified because we do not have quantitative data on the frequency of product labeling changes that would change prescribing practices. Moreover, we are unable to determine how often health care professionals rely on the prescribing information as well as different information sources, such as journal articles, trade press, colleagues, "Dear Health Care Provider" letters, postings on FDA's Web site, and sales representatives to learn about changes or updates in drug information.

Based on 11 years of data (2003 to 2013), there are about 500 safety labeling changes made each year. FDA tracks safety labeling changes and classifies them by type, depending on the risk described and the section of the prescribing information that is changed. For example, changes to a boxed warning or the "Contraindications" section can affect prescribing decisions and the size of the patient population eligible for the drug, while changes to warnings, precautions, and adverse events can affect patient monitoring or management. Based on an internal review of changes to the boxed warning and "Contraindications" sections between the years 2003 to 2013, we found that there are about 50 changes or additions to the boxed warning and about 60 additions or changes to the "Contraindications" section each year.

D. Risk Analysis

The paper prescribing information that accompanies drugs has many recognized drawbacks for communicating information in addition to the potential of being out-of-date. The major drawbacks are that it is printed in small font (generally 6 point) on thin, oversized paper

that has to be folded multiple times to fit on top of a drug container or within a carton. To access the information the prescribing information must first be removed (some are attached with plastic binding) and unfolded, then searched to find where the desired information is. The paper cannot be reattached to the container once removed and may be difficult to return to a carton. If multiple prescriptions would be filled from a single container, the paper prescribing information would need to be stored in some manner separate from the product for future reference. The electronic version would allow the user to adjust the font size and because it is in SPL format, would allow the user to jump to the section of the document they were interested in consulting. We envision that hospitals and chain pharmacies as well as third party suppliers offering electronic compendia will download the prescribing information and update it regularly. Their employees or clients would not actually go to the internet to obtain the prescribing information but access it through existing computer systems.

We are aware that transitioning from a paper to electronic delivery system for information is a change in practice that could pose some tradeoff in public safety under certain circumstances. To examine the potential for harm if the prescribing information no longer accompanied the product in paper form we considered the tradeoff users would face under different settings. Eastern Research Group, Inc. (ERG) estimated that pharmacists refer to product labeling less than 1 percent of the time when filling prescriptions and it could add up to 10 minutes if they were to access the internet and print the information. (Ref. R1). In their estimate they did not consider the time savings a pharmacist might have finding the information in the electronic document versus the paper version or a non-internet based electronic version, which we believe most businesses will use. Anytime a pharmacist accesses the prescribing information there is a disruption in workflow, but this change in practice could lead some to rely

more heavily on memory or access a compendia that may not have the most current prescribing information. Relying on memory or on outdated prescribing information could result in harm. Relying on a paper compendia rather than the electronic version would be like relying on the paper prescribing information and take very little extra time but could be even less current than the paper prescribing information would have been. We request comment on the extent to which pharmacists may rely on memory or possibly outdated paper versions of the prescribing information and the relationship to the potential for harm.

Because physicians and nurses generally do not dispense drugs, they would not ordinarily have access to the drug containers and packaging that would contain the paper prescribing information. Physicians and nurses generally rely on electronic or paper compendia when they need to access the prescribing information. We foresee no change in practice or workflow disruption if this rule should be finalized as proposed.

In an emergency, each situation would present a unique set of circumstances. In a widespread natural disaster, one would expect limited access to electricity, internet connectivity problems, and communication disruption making access to the label repository or the viability of faxing documents unfeasible. We spoke with first responders in the US Public Health Service who have deployed to recent natural disasters and they typically arrive fully equipped with the medicines they are going to dispense and bring compendia and mobile wireless capability. They have trained extensively for such situations and are very familiar with the limited drugs they are dispensing, reducing the risks associated with not having access to the electronic prescribing information. Thus, if these responders' experiences are representative, reference to the full content of labeling would rarely be necessary in such an emergency.

Another emergency would be a widespread power outage that could affect telephone lines as well as electrical power. When it comes to natural disasters that affect pharmacies, they often have contingency plans in place for how services will be provided (e.g., during events such as power disruptions). For example, some pharmacies may rely on back-up generators or refer patients to another nearby pharmacy.

E. Who Will Be Affected?

The proposed rule will affect both those responsible for creating and providing the content of the prescribing information and the users of the information. Drug manufacturers, repackers, relabelers, and manufacturers or repackers of private label drugs would incur short-term costs to put new labels on the products' immediate container label and outer container or package. In the long run, however, the costs of producing prescribing information will decrease because these manufacturers would no longer need to provide it in paper form. Health care professionals, mainly physicians and pharmacists, could incur both short-run and long-run costs as a result of the proposed rule. The short-run costs would result from acquiring extra computers or printers where necessary. The long-run costs would result from the costs to print the prescribing information when necessary and the need for greater search time or interruption in workflow for pharmacists. Although the costs and cost savings will initially be incurred by drug manufacturers, as well as physicians and pharmacists, these market changes will also affect others. We are, however, unable to estimate the distribution of costs and cost savings across the affected markets.

Distributors and wholesalers of prescription drugs will also benefit from the proposed rule because less space would be required to store product inventory and fewer disruptions in workflow due to dislodged or missing product labeling would occur. Printing companies who

specialize in printing and folding product labeling will lose a substantial amount of their business, and many may have to develop new lines of work to remain in business.

There are three major manufacturers of thin paper and a few smaller manufacturers that may specialize in making thin paper. The prescribing information accounts for about 30% of the market for thin paper. Thin paper is also used for phone books, bibles, cosmetic inserts, and financial and congressional reports. Manufacturers should be able retool their equipment to produce other types of paper.

There are 40 to 50 printers that specialize in printing on large sheets of thin paper. While most printing machines can be repurposed for other types of printing, the folding and binding machines are highly specialized and predominately used for pharmaceutical inserts. Should this proposed rule finalize as proposed, there would still be limited demand for folded and bound printed inserts for drugs that require patient package inserts and some cosmetics. We did not estimate these distributional effects of the proposed rule.

To estimate baseline practices and the cost and savings of this proposed rule we contracted with the consulting firm ERG. (Ref. R1) What follows combines a summary of ERG's findings with additional analysis of the costs and savings to manufacturers of blood and blood components.

Data on many of the variables necessary to estimate the costs and cost savings are not collected, so ERG relied on the professional literature, expert opinion, and small published surveys to impute the values. Because of the uncertainty around some of the estimates, we report large ranges for some values in this analysis. We request comment on the methods and estimates used for this analysis.

Because the economic impact of the proposed rule differs substantially for the providers and the users of the prescribing information, we discuss them separately. The first section will discuss the economic effects on the providers of prescribing information, which includes drug manufacturers, repackers, relabelers, and contract manufacturers. The second section will discuss the economic effects on the users of the prescribing information, health care professionals. We assess the impact of the proposed rule on manufacturers of blood and blood component products in a third section because the regulatory requirements and use of blood and blood component products differ substantially from other drug and biological products.

We did not assess the impact of the proposed rule on private practitioners or professional organizations representing such practitioners, and we invite comment on how this rule may impact groups outside of those included in this assessment.

F. Providers of Prescribing Information

The proposed rule would require changing the product label on the immediate container label and any outer container or outside package to include a statement that directs users to FDA's labeling repository Web site to access current prescribing information and a toll-free telephone number for requesting alternative options for obtaining the prescribing information. If the proposed rule becomes final, manufacturers that market products would have up to 2 years to relabel their products, submit updated prescribing information, and ensure that the prescribing information available in the labeling repository is current. Currently, prescribing information and other components of product labeling must be submitted in SPL format when listing drug products with the Agency under part 207. Most products would be in compliance with this requirement. Applicants or manufacturers of products that require marketing applications have been required to submit the prescribing information in this format since October 2005, and we

assume they regularly validate the accuracy and completeness of any new posting to FDA's repository as a part of good business practice and for product liability reasons. Repackers and relabelers have only been required to submit prescribing information electronically since June 2009. The SPL format is not mandatory under current requirements for the repackaged, relabeled, and private label products until the prescribing information that was listed at the time the requirement went into effect is revised. Given that this proposed requirement would go into effect sometime in the future, we assumed that all repackers and relabelers would have been required to submit their prescribing information in the electronic format before a final rule went into effect. However, they may not have verified the accuracy and completeness of the postings prior to a final rule and could incur additional one-time costs.

ERG used data from FDA's drug registration and listing databases to estimate the number of manufacturers affected by this proposed rule. Because of the way the data was collected, the registration and listing information were kept in separate databases. As a result, it was not clear if manufacturers were categorized consistently, and therefore there may be double counting of some firms or products and counting of some products that are not currently marketed.

FDA estimates that the proposed rule would affect between 551 and 700 manufacturers of NDA, BLA, and ANDA prescription drug products and from 900 to 1,300 repackers, relabelers, and manufacturers or repackers of private label products (table 3).

Table 3--Firms, SKUs and Prescribing Information Affected

	Small Manufacturers of Branded Drugs[1]		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, Makers of Products for Private Label Distribution	
	Low	High	Low	High	Low	High	Low	High
No. of firms	163	207	156	198	232	295	900	1,300
No. of SKUs	7,500	12,500	7,500	12,500	15,000	25,000	120,000	150,000

No. of units of prescribing information produced annually (millions)	59.7	80.7	238.7	322.9	298.4	403.7	1,613.3	2,182.7

[1]The Small Business Administration defines small as fewer than 500 employees for biological product firms and fewer than 750 for drug firms.

Most of the costs will be one-time costs to change the product label on the immediate container and outer container or package to include a statement that directs users of the prescribing information to FDA's labeling repository Web site and to the toll-free number as an alternative source for prescribing information if the Internet is not available. There would be annual costs to change to nonstandard forms of labels for some products whose containers are too small to fit the required Web site address and toll-free number statement. There would also be annual costs for maintaining the automated toll-free phone number.

G. Cost to Change Labels on Immediate Container Labels and Outer Containers or Packages

Some of the costs per label change would be accrued per firm; these include administrative costs such as meetings to discuss the requirements in the regulation and to decide how to meet them. Other costs would be accrued per SKU, which is the number of individual package sizes. These costs include the artwork and plates for printing the new product labels for the immediate container label and outer container or package, the inventory loss of old labels, and manufacturing hours to make changes to the production line. Costs will also differ by size and type of firm. Table 3 lists the number of firms by type and size and ERG's estimates of the average number of SKUs produced by each type of firm.

The one-time administrative costs per firm to change the product label on the immediate container label or outer container or package range from $140 for repackers and relabelers to $2,516 for large manufacturers of branded products (see table 4). The lower estimate for the

costs per firm for the repackers and relabelers assumes that there would be no need for interdepartmental meetings across these firms because they are basically reproducing the content of a manufacturer's labeling and would approach all of the labeling changes in a similar manner. The one-time costs to change the immediate container label per SKU by firm type range from $684 for repackers and relabelers to $1,590 for large manufacturers of branded products. The one-time costs to change the label on the outside packaging per SKU by firm type range from $1,300 for generic drug manufacturers to $2,800 for large manufacturers of branded products. The total one-time costs to change labels on the immediate container label and outer container or package for the 150,000 to 200,000 SKUs affected by this proposed rule would be $134.7 million to $214.5 million (see table 4).

Table 4.--One-Time Costs to Change Immediate Container Labels and Outer Containers or Packages*

	Small Manufacturers of Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, Makers of Products for Private Label Distribution		Total	
	Low	High	Low	High	Low	High	Low	High	Low	High
Administrative costs per firm ($)	1,409	1,409	2,516	2,516	1,610	1,610	140	140		
No. of firms	163	207	156	198	232	295	900	1,300		
Container label change cost per SKU ($)	726	726	1,590	1,590	750	750	684	684		
Outer package label change cost per SKU ($)	1,300	1,300	2,800	2,800	1,300	1,300	1,384	1,384		
No. of SKUs with outer package	2,250	5,000	2,250	5,000	4,500	10,000	6,000	22,500		
No. of SKUs	7,500	12,500	7,500	12,500	15,000	25,000	120,000	150,000		
Total label change costs ($ millions)	8.6	15.9	18.6	34.4	17.5	32.2	90.0	132.0	134.7	214.5

*Sums may not add due to rounding.

H. Nonstandard Forms of Product Labels for the Immediate Container Labels and Outer Containers or Packages

To estimate the cost for the SKUs with container labels too small to accommodate the text of the proposed statement, ERG assumed firms would use a nonstandard label, such as a pull-back or peel back label. Firms could choose to increase the size of the immediate containers or outer containers or packages, but in most cases those options would be more expensive. Firms adding nonstandard labels would incur both one-time and recurring costs. The one-time costs include the costs for additional meetings, artwork, printing plates, and changes to the packaging line. The recurring costs would be the difference between the costs of the current label and adding the nonstandard label. ERG based its estimates of these costs on expert opinion and assumed that 10 to 15 percent of the SKUs would require a nonstandard label. The one-time costs per firm to change to a nonstandard label are listed in table 5 and are about $3,600 to $3,700 for all firm types except large manufacturers of branded products, who would have a unit cost of $4,663. For annual recurring costs, ERG estimated that the nonstandard label would cost an additional $0.02 to $0.03 per label. To calculate the recurring costs ERG needed an estimate of the number of labels that would be used annually, which is based on the annual sales volume per SKU. This information is not collected in a format they could use for their calculations, so they derived their estimates from the number of SKUs by type of firm and an estimate of the total number of prescribing information inserts produced annually. The ranges for the number of labels per SKU are listed in table 5, along with the unit annual costs. Total one-time costs for the nonstandard labels range from $54.7 million to $109.8 million and the annually recurring costs range from $5.5 million to $20.4 million.

Table 5.--One-Time and Annual Costs for Nonstandard Labels

	Small Manufacturers Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, and Products for Private Label Distribution		Total	
	Low	High	Low	High	Low	High	Low	High	Low	High
One-time cost per SKU ($)	3,705	3,705	4,663	4,663	3,745	3,745	3,565	3,565		
Incremental cost per label ($)	0.03	0.03	0.02	0.02	0.02	0.02	0.03	0.03		
Units per SKU relabeled	10,000	20,000	50,000	75,000	30,000	40,000	10,000	20,000		
No. of SKUs that cannot accommodate proposed text	750	1,875	750	1,875	1,500	3,750	12,000	22,500		
Total one-time costs ($ millions)	2.8	6.9	3.5	8.7	5.6	14.0	42.8	80.2	54.7	109.8
Annual costs ($ millions)	0.2	1.1	0.8	2.8	0.9	3.0	3.6	13.5	5.5	20.4

I. Toll-Free Telephone Number

Firms will be required to maintain a toll-free number that users of prescribing information can call if they do not have Internet access. Firms would likely use their existing automated telephone infrastructure but would need to add an option so that someone could request that the prescribing information be mailed, faxed, or emailed to them. ERG concluded that the toll-free telephone number would not change frequently, as that would require the production of new labels for the immediate container and outside package. The costs to comply with this requirement would include labor costs to modify the phone system and to respond to any requests. Because firms would be using existing phone systems, ERG determined the one-time costs to set up the toll-free number would be negligible. ERG projected the number of requests firms might receive would range from 5 to 10 per month for small manufacturers of branded products and repackers and relabelers to 50 to 150 per month for large manufacturers of

branded drugs (table 6). Annual unit costs for fielding requests for prescribing information ranged from $9 to $19 dollars for small manufacturers of branded drug products and repackers and relabelers to $113 to $338 for large manufacturers of branded drug products. ERG also assumed that about 50 percent of firms would have automated call handling systems that would reduce the unit costs by half. The total annually recurring costs for maintaining the toll-free phone number would range from $26,500 to about $90,740. Table 6 lists the total annually recurring costs by firm type.

Table 6.--Annual Cost to Maintain Toll-Free Number

	Small Manufacturers of Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, and Private Label Distribution		Total	
	Low	High	Low	High	Low	High	Low	High	Low	High
No. of calls per month per firm	5	10	50	150	10	20	5	10		
Unit costs per firm	$9	$19	$113	$338	$20	$40	$9	$19		
No. of firms	163	207	156	198	232	295	300	433		
Total annual costs	$1,525	$3,881	$17,533	$66,946	$4,630	$11,786	$2,813	$8,125	$26,501	$90,738

J. Verification of SPL Submissions for Repackers and Relabelers

The proposed rule would require that every prescription drug product marketed have the most current version of its prescribing information submitted to FDA in an electronic format that FDA can process, review, and archive (currently SPL format) by the compliance date. Manufacturers that are sponsors of market applications are already required to submit the content of their current prescribing information in an electronic format that FDA can process, review, and archive (currently SPL format) to FDA, and because we upload them to our drug label

repository, they verify the accuracy and completeness of the prescribing information after it is posted. Repackers and relabelers and private label distributors have only recently been required to submit prescribing information in SPL format. Currently, these firms can postpone submitting the SPL file until there is a change in the prescribing information that was submitted at the time of drug listing. All repackers and relabelers will likely have submitted the prescribing information in an electronic format by the effective date should this proposed rule become final. Because the repackers and relabelers are not the authors of the content of the prescribing information, they may not have reviewed the accuracy and completeness of the posted prescribing information. To account for this cost, we assumed that all repackers and relabelers would need to review the posted prescribing information for their products and that the review would take about 5 hours for each document. We assumed that 80 percent of the prescribing information for products marketed by repackagers and relabelers would need to be reviewed for accuracy and completeness before the products can be shipped accompanied by the electronic label. The total one-time cost to review the initial submission of prescribing information to the repository would range from $2.0 million to $2.5 million assuming 20,000 to 25,000 separate pieces of prescribing information produced by repackagers and relabelers and a wage rate of $25[1] (20,000 x 0.80 x $25 wage x 5 hours and 25,000 x .80 x $25 wage x 5 hours) (table 7).

Table 7.--One-Time Cost to Repackers and Relabelers for Initial Verification of Electronic Submission

	Low	High
No. of prescribing information files affected	20,000	25,000
Cost to review electronic submission	$125	$125
Total one-time costs ($ millions)	$2.0	$2.5

[1] Wage derived from 2010 Bureau of Labor Statistics Occupation Employment Statistics Survey, occupation code 43-9081 proofreader for legal services – mean wage rate = $17.73 + 40 percent for nonwage benefits = $24.82, rounded to $25, at http://www.bls.gov/.

K. Total Annual Costs for Providers of Prescribing Information

The total one-time and annual costs that providers of prescribing information would incur are listed in table 8; the one-time costs would range from $191.4 million to $326.7 million and annual costs would range from $5.5 million to $20.5 million. Changing the immediate container label and outer container or package accounts for most of the one-time costs, and the impact per firm would vary based on the number of SKUs. The majority of the recurring costs would be for using nonstandard labels on immediate container labels or outer container or packages that are too small to accommodate the proposed label statement containing the link to the FDA's labeling repository Web site address and the toll-free telephone number.

Table 8.--Summary of One-Time and Annual Cost to Providers of Prescribing Information ($ millions unless noted)

	Small Manufacturers of Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, and Products for Private Label Distribution		Total	
	Low	High	Low	High	Low	High	Low	High	Low	High
One-time costs:										
Cost to change immediate container label and outside package	8.6	15.9	18.6	34.3	17.5	32.2	90.0	132.0	134.7	214.5
Nonstandard label	2.8	6.9	3.5	8.7	5.6	14.0	42.8	80.2	54.7	109.8
Review electronic submission							2.0	2.5	2.0	2.5
Total one-time costs									191.4	326.7
Annual costs:										
Nonstandard label	0.2	1.1	0.8	2.8	0.9	3.0	3.6	13.5	5.5	20.4
Maintain toll-free number ($ dollars)	1,525	3,881	17,533	66,946	4,630	11,786	2,813	8,125	26,501	90,738
Total annual costs									5.5	20.5

L. Savings to Providers of Prescribing Information From No Longer Providing the Paper Form

The providers of prescribing information would realize substantial savings from no longer having to store and print the paper form of prescribing information. ERG estimated that average costs to print and fold the paper forms of prescribing information range from $0.03 to $0.07 and the per SKU storage cost ranges from $1.40 to $1.50, based on storage costs of about $5 per square foot. There would also be savings from no longer losing labeling inventory when there are changes to the prescribing information. Because the factors that would affect the amount saved per change are highly variable, however, ERG could not develop an estimate for inventory savings. Table 9 lists the variables used for the calculation of annual savings. For the entire industry, annual cost savings would range from $93.8 million to $216.6 million.

Table 9: Savings to Providers of Prescribing Information

	Small Manufacturers of Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, and Products for Private Label Distribution		Total	
	Low	High	Low	High	Low	High	Low	High	Low	High
Number of Firms	163	207	156	198	232	295	900	1300		
Number of SKUs	7,500	12,500	7,500	12,500	15,000	25,000	120,000	150,000		
Number of PIs produced annually ($millions)	59.7	80.7	238.7	322.9	298.4	403.7	1,613.3	2,182.7		
Annual storage cost per insert	$1.40	$1.40	$1.50	$1.50	$1.50	$1.50	$1.40	$1.40		
Storage costs	$10,500	$17,500	$11,250	$18,750	$22,500	$37,500	$168,000	$210,000		
Printing and folding ($millions)	$2.7	$6.1	$8.1	$20.7	$10.1	$25.8	$72.6	$163.7		
Total annual savings	$2.7	$6.1	$8.1	$20.7	$10.2	$25.9	$72.8	$163.9	$93.8	$216.6

	Small Manufacturers of Branded Drugs		Large Manufacturers of Branded Drugs		Generic Drug Manufacturers		Repackers, Relabelers, and Products for Private Label Distribution		Total	
($millions)										

M. Net Cost Savings for Providers of Prescribing Information

We estimate the net effect of the proposed rule on the cost of providing prescribing information by subtracting the costs from the savings. To compare the one-time and annual costs and savings for providers of prescribing information over time, we annualized the one-time costs using discount rates of 7 and 3 percent over a 10-year period (table 10). The annualized costs were then added to annual costs for total annualized costs of $32.8 million to $67.0 million at the 7 percent discount rate, and $27.9 million to $59.8 million at the 3 percent discount rate. The difference between the annual savings and annualized costs would be a net annual savings to providers of $61.0 million to $149.6 million at the 7 percent discount rate and $65.9 to $157.8 at the 3 percent discount rate.

Table 10.--Net Savings to Providers of Prescribing Information ($ millions)

	7 % discount rate, 10 years		3 % discount rate, 10 years	
	Low	High	Low	High
Annualized one-time costs	$27.3	$46.5	$22.4	$38.3
Annual cost	$5.5	$20.5	$5.5	$20.5
Total	$32.8	$67.0	$27.9	$59.8
Annual savings	$93.8	$216.6	$93.8	$216.6
Net savings*	$61.0	$149.6	$65.9	$157.8

*Net savings is calculated by subtracting the lowest costs within a range from the lowest savings and the highest costs from the highest savings. An alternative, more robust estimate is given in table 19.

N. Users of Prescribing Information

It is difficult to estimate the effects of the electronic distribution of prescribing information on health care professionals because once they become familiar with a drug product they may not need to refer to the prescribing information for routine prescribing and dispensing. A failure to refer to the prescribing information could therefore reflect either prior use or habitual non-use. Our estimates of how often the prescribing information would be referenced and printed are based on small surveys or the opinion of experts. We also cannot predict how the availability of electronic forms of the prescribing information for all drug products from one source will change the products or services offered by the venders of compendiums and prescribing software or how the electronic availability will decrease the costs of searching for prescribing information. Another uncertainty is how health care professionals will respond to the change. While this rule has specific requirements for manufacturers to follow, the changes under this regulation do not impose new requirements on the practice of the prescribers and dispensers (physicians and pharmacists), which is also regulated by the States. For this analysis, we assume that pharmacists will continue to use the prescribing information as a key source of drug product information and make any necessary changes to ensure they have access to the most current version. However, there are a number of alternative scenarios that could develop that could provide the information more efficiently. ERG found that most physicians do not use the paper form of the prescribing information but instead use compendiums containing information supplied by third parties. We assume that the physicians would not change their behavior and start searching the FDA's labeling repository Web site for drug information. We expect the third party information providers would use the FDA's labeling repository Web site as the source of the most current prescribing information and updates. We ask for comments from health care

professionals as to how this proposed rule would change how they obtain prescribing information.

Most pharmacies use software programs when filling prescriptions that print out the patient's label and either flag or print out the appropriate warnings or other patient information that needs to be attached to the patient's prescription container. It is possible that once there is a single source for complete and free access to all drug products' prescribing information, they might begin to include a message that would notify the pharmacist when the prescribing information has changed and provide easy electronic links to access it in a more convenient format. While physicians do not regularly consult the paper form of the prescribing information now, the third party vendors of medical product information that physicians use may start using the electronic prescribing information as their source for the information, which would be the most current when compared with the paper forms. The vendors may start to provide timely updates that could even be included in electronic prescribing software. Value-added services like these would increase the public health benefits of the electronic distribution of prescribing information because these services could alert the health care professional to changes in the prescribing information at the time of prescribing and dispensing.

The proposed rule would lead to greater costs for pharmacies than for other potential users of the prescribing information. These costs include one-time costs to acquire the infrastructure to access the electronic version of the prescribing information and to be able to print them when necessary. The annual recurring costs would be to maintain the infrastructure and to print some prescribing information. These costs represent a transfer of some printing responsibilities from drug manufacturers to pharmacies.

Table 11 shows the number of entities that use the prescribing information and would be potentially affected by the proposed rule. There are about 79,000 pharmacies, which ERG subcategorized as retail chain stores, independent pharmacies, hospital pharmacies, and other institutions that purchase and dispense drug products. The other category includes nursing homes; home health care providers; mail order pharmacies; and other institutions such as schools, prisons, and clinics. There are also about 377,000 physicians who regularly prescribe drugs that could potentially be affected.

Table 11.--Number of Potential Users of Prescribing Information Affected

Chain Drug Stores Headquarters	244
Chain Stores (drug, grocery, mass merchandise)	38,695
Independent Pharmacies	16,921
Hospital Pharmacies	10,362
Other Institutions	12,984
Prescribing Physicians	377,213

O. Computer and Printer Needs

Based on consultation with industry trade associations and industry experts, ERG determined that all pharmacies have computers that are used for nondispensing activities. Most also have printers that could be used for printing the prescribing information when necessary without a disruption of other work activities. Lacking a reliable estimate of the number of pharmacies that would need to purchase additional printer capacity, ERG assumed that 33 percent might need to purchase additional printers at a cost of $100 to $400, and perhaps 1 percent may need to purchase additional computers that range in cost from $400 to $700. The total one-time cost for additional hardware ranges from $2.4 million to $9.1 million, and there would be annual recurring maintenance costs associated with the equipment equal to 10 percent of the cost of the equipment, ranging from about $244,200 to about $917,100 for all pharmacies

(table 12). Other institutions and prescribing physicians would not incur additional costs for printers or computers because they currently do not use the prescribing information in paper form.

Table 12.--Cost of Hardware

	Chain Pharmacies		Independent Pharmacies		Hospital Pharmacies		Total	
	Low	High	Low	High	Low	High	Low	High
Cost of laser printer	$100	$400	$100	$400	$100	$400		
Maintenance of printer	$10	$40	$10	$40	$10	$40		
Percent needing printer	33%	33%	33%	33%	33%	33%		
Cost of computer	$400	$700	$400	$700	$400	$700		
Maintenance of computer	$40	$70	$40	$70	$40	$70		
Percent needing computer	1%	1%	1%	1%	1%	1%		
No. of establishments affected	38,695	38,695	16,921	16,921	10,262	10,262		
Total one-time costs ($ millions)	$1.4	$5.4	$0.6	$2.3	$400,000	$1.4	$2.4	$9.1
Total annual costs	$143,172	$537,861	$62,680	$235,202	$38,339	$144,032	$244,191	$917,095

P. Training of Pharmacy Staff

ERG assumed the training costs would be minimal, between 15 and 30 minutes per pharmacist because most pharmacists are very familiar with how to access the Internet and how to search for information. Once trained, there would be no need for follow-up or recurring training of pharmacists. ERG assumed that about 3 pharmacists per pharmacy would be trained in chain and independent pharmacies, and 11 pharmacists in hospital pharmacies. Total one-time costs for training are presented in table 13 and range from $4.8 million to $9.5 million.

Table 13.--Training Costs

	Chain Pharmacies		Independent Pharmacies		Hospital Pharmacies		Total	
	Low	High	Low	High	Low	High	Low	High
No. hours per staff	0.25	0.5	0.25	0.5	0.25	0.5		
No. pharmacists trained per establishment	3	3	3	3	11	11		
Unit cost per pharmacy	$51	$102	$51	$102	$187	$374		
Total one-time costs ($ millions)	$2.0	$3.9	$0.9	$1.7	$1.9	$3.9	$4.8	$9.5

Q. Internet Access

ERG found that essentially all pharmacies have Internet access but that some retail chains and hospitals partially or totally block employee access. ERG estimated that about 26 percent of the retail chains would have to make changes so the individual stores could have free access to the FDA's labeling repository Web site, which would require about 3 to 8 hours of the network administrator's time. The incremental annual cost for the entire retail chain sector would range from $10,043 to $26,781. ERG estimated that about one-half of hospitals restrict access to the Internet for their pharmacists. Assuming it would require the same number of labor hours to maintain open access for hospitals as it was for the retail chain pharmacies (3 to 8 hours), the total cost for hospitals ranges from $0.8 million to $2.2 million (table 14). Independent pharmacies were assumed to have unlimited Internet access.

Table 14.--Internet Access

	Chain Pharmacies		Hospital Pharmacies		Total	
	Low	High	Low	High	Low	High
No. of hours system administrator	3	8	3	8		
Unit annual cost	$159	$425	$159	$425		
Percent establishments with blocked access	26%	26%	50%	50%		
Total annual cost	$10,043	$26,781	$826,000	$2,202,667	$836,043	$2,229,448

R. Time Lost Due to Accessing and Internet Delays

Accessing the prescribing information over the Internet could take more time than removing it from the immediate container label or outer container or package. To estimate these costs, ERG combined information from the few studies on pharmacist's usage of the prescribing information with expert opinion to estimate the number of times pharmacists would consult the prescribing information either for their own reference or in response to a customer inquiry, and the average amount of time it would require. We expect time lost due to accessing the Internet to be negligible for infrequent users of the prescribing information. ERG's estimates, presented in table 15, show that chain and independent pharmacists would consult the prescribing information about 88 times per year and would print it one-third to two-thirds of the time, with a 10-minute delay occurring about 10 percent of the time. Pharmacists in hospital settings were estimated to consult the prescribing information more often, about 156 times per year. ERG used the same estimates of printing between one-third to two-thirds of the prescribing information consulted and experiencing delays about 10 percent of the time. The total estimated annual cost for time delays ranges from $31.9 million to $39.8 million.

Table 15.--Accessing and Printing Delays

	Chain Pharmacies		Independent Pharmacies		Hospital Pharmacies		Total	
	Low	High	Low	High	Low	High	Low	High
Frequency pharmacists consults prescribing information	88	88	88	88	156	156		
Expect frequency to print prescribing information	29	58	29	58	52	104		
Annual No. of delays per pharmacist	12	15	12	15	21	26		
Delays in minutes	10	10	10	10	10	10		
Unit cost per pharmacist	$132	$165	$132	$165	$236	$295		
No. of pharmacists working at a given time, per pharmacy	3	3	3	3	4	4		
Unit annual cost per establishment	$397	$496	$397	$496	$943	$1,178		
Total annual cost ($ millions)	$15.4	$19.2	$6.7	$8.4	$9.8	$12.2	$31.9	$39.8

S. Printing Costs

There would also be an annual cost in materials for some printing by users of the prescribing information. We assumed that users would print the entire 20 to 30 pages of the prescribing information in the currently available format at a materials cost of $.04 per page and 30 to 60 seconds of labor. ERG used the same unit cost estimate, $1.37 to $2.33, for all users except physicians; the unit cost for physicians, $1.88 to $3.35, is higher due to higher labor costs. ERG assumed that infrequent users might print the prescribing information 4 to 8 times per year. The detailed estimates are presented in table 16; the total annual cost of printing for all users of the prescribing information would be from $12.2 million to $43.1 million.

Table 16.--Printing Costs

	Chain Pharmacies		Independent Pharmacies		Hospital Pharmacies		Physicians		Other Institutions	
	Low	High	Low	High	Low	High	Low	High	Low	High
Frequency of printing	29	58	29	58	52	104	4	8	4	8
Unit cost to print	$1.37	$2.33	$1.37	$2.33	$1.37	$2.33	$1.88	$3.35	$1.37	$2.33
Cost per pharmacist or physician	$40	$136	$40	$136	$71	$243	$8	$27	$5	$19
Cost per pharmacy	120	408	120	408	284	971	$8	$27	$5	$19
Total annual cost by user category ($ millions)	$4.6	$15.8	$2.0	$6.9	$2.9	$10.1	$2.8	$10.1	$0.1	$0.2
Total annual cost all users ($ millions)	Low estimate: $12.2		High estimate: $43.1							

T. Total Cost for Users of the Prescribing Information

The total one-time and recurring costs to potential users of the prescribing information

are given in table 17. One-time costs ranged from $7.2 million to $18.6 million. Annual costs ranged from $45.4 million to $86 million. The estimated costs were driven by delays in accessing and printing and the number of units of prescribing information that would be printed rather than read on a computer screen. Annualized one-time costs over 10 years range from $1.0 million to $2.6 million at the 7 percent discount rate and from $0.8 million to $2.2 million at a 3 percent discount rate. The total annualized costs are the sum of the annualized one-time costs and the annual costs, and range from $46.4 million to $88.7 million at the 7 percent discount rate and from $46.2 million to $88.2 million at a 3 percent discount rate, as shown in table 18.

Table 17.--Summary of One-Time and Annual Costs for Users of Prescribing Information ($ millions)

	Chain		Independent		Hospital		Physician		Other Institutions		Total All Users	
	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
Hardware	$1.4	$5.4	$0.6	$2.3	$0.4	$1.4					$2.4	$9.1
Training	$2.0	$3.9	$0.9	$1.7	$1.9	$3.9					$4.8	$9.5
Total one-time costs	$3.4	$9.3	$1.5	$4.0	$2.3	$5.3					$7.2	$18.6
Annual costs:												
Hardware	$0.1	$0.5	$0.06	$0.2	$0.04	$0.1					$0.2	$0.9
Internet access	$0.01	$0.03	$0	$0	$0.8	$2.2					$0.8	$2.2
Access and printing delays	$15.4	$19.2	$6.7	$8.4	$9.8	$12.2					$31.9	$39.8
Printing costs	$4.6	$15.8	$2.0	$6.9	$2.9	$10.1	$2.8	$10.1	$0.1	$0.2	$12.2	$43.1
Total annual costs	$20.2	$35.6	$8.8	$15.5	$13.6	$24.6	$2.8	$10.1	$0.1	$0.2	$45.4	$86.0
Worst case scenario: Average annual cost per affected entity (dollars)	$565	$1,014	$565	$1,014	$1,436	$2,684	$8	$27	$5	$19		

Table 18.--Annualized Costs for Users of Prescribing Information ($ millions)

	7% discount rate, 10 years		3% discount rate, 10 years	
	Low	High	Low	High
Annualized one-time costs	$1.0	$2.6	$0.8	$2.2
Annual cost	$45.2	$86.0	$45.2	$86.0
Annualized cost to users	$46.4	$88.7	$46.2	$88.2

U. Manufacturers of Blood and Blood Component Products

The proposed rule would modify the labeling requirements for blood and blood component products under 21 CFR part 606. To meet the requirement that the Circular of Information be available for electronic distribution with blood and blood component products, blood manufacturers would incur one-time costs to change the labels on the immediate containers of blood and blood component products to include a statement that directs users of the information to FDA's labeling repository Web site and to the automated toll-free number as an alternative source for the Circular of Information if the Internet is not available. The blood manufacturers would also have annually recurring cost savings from no longer having to provide the Circular of Information in paper form.

There are 118 licensed manufacturers with 1,508 facilities and 1,084 registered manufacturers of blood and blood component products.[2] To estimate the one-time cost to change the label on the immediate containers, we estimated that each licensed and each registered manufacturer would have to change 5 labels for a total of 6,010 label changes ((118 + 1,084) x 5). We estimated that the cost to change the labels would range from $600 to $725 per product and that the addition of the proposed statement would not require an increase in the size of the container label. The total one-time cost to relabel blood and blood component products would range from $3.6 million to $4.3 million (6,010 labels x $600 or 6,010 labels x $725). The one-time costs annualized at a 7 percent discount rate over 10 years would be $0.5 million to $0.6

[2] Source: FDA registration database.

million; using a 3 percent discount rate over 10 years would result in costs of $0.4 million to $0.5 million.

Estimating the savings to blood and blood component manufacturers is difficult because we do not know how many circulars are distributed with the blood and blood component products. Most manufacturers purchase the Circular of Information from the American Association of Blood Banks (AABB) for $40 to $50 per 100 circulars, depending on their membership status with the association. Based on sales information provided to us by AABB, about 1,630 orders for the circular were filled in a 12-month period. To estimate the total number of circulars for all blood manufacturers we inflated the AABB orders by 5 percent and assumed that the manufacturers that do not purchase from AABB would incur the same costs for the circulars they distribute. Using the midpoint of $45 for the average cost of an order of 100, the annual savings from not needing to supply the circular in paper form would be $76,950 ($45 x 1,710).

We estimate the net costs as the difference between the annual savings and the annualized costs. The annualized costs would range from $0.4 million ($0.5 million - $76,950) to $0.5 million ($0.6 million - $76,950) per year when one-time costs are discounted at 7 percent over 10 years. When the one-time costs are discounted at a 3 percent rate over 10 years, the annualized costs ranged from $0.3 million ($0.4 million - $76,950) to $0.4 million ($0.5 million - $76,950).

The impact of electronic distribution of the Circular of Information on users would likely be insignificant. Because the information in the circular covers all blood and blood components and does not change often, users are familiar with the information, and an electronic version should not increase the search time or require the purchase of special equipment not already available to the user. We request comment on this conclusion.

We did not include the cost for each blood and blood components manufacturer to electronically submit and review the Circular of Information since the information is the same for all firms and for all blood and blood component products. Rather than 1,200 firms submitting and verifying the identical information, we believe a simpler means of compliance with the rule will be found. If each manufacturer were required to electronically submit and review the circular for accuracy and completeness of the submission it would cost an additional $150,000 (1,200 Circulars x $125 to review) for the review and $30,000 for the initial electronic submission (1,200 Circulars x 0.5 hours x $50 wage) for a total additional cost of $180,000, which is about a 5 percent increase in the one-time costs estimated to be incurred by blood and blood component manufacturers.

V. Total Costs and Savings of the Proposed Rule

Depending on the values of the variables used in the analysis, the proposed rule could have an annualized net savings of $5.0 million to $73.5 million at a 7 percent discount rate and $10.0 million to $82.2 million at a 3 percent discount rate (see table 19). These totals do not include the public health benefits of users having access to the most up-to-date versions of the prescribing information.

Table 19.--Summary of Annualized Costs and Cost Savings of the Proposed Rule ($ millions)

	7% discount rate, 10 years		3% discount rate, 10 years	
	Low	High	Low	High
Savings (net) to providers of drug labels*	$51.8	$162.7	$56.6	$170.8
Costs to users	$46.4	$88.7	$46.2	$88.2
Costs to blood manufacturers	$0.4	$0.5	$0.3	$0.4
Net savings	$5.0	$73.5	$10.0	$82.2

*These net savings differ from table 10 due to alternative calculation method subtracting highest costs within a range from the lowest savings and lowest costs from highest savings rather than subtracting low numbers from low and high from high.

The savings that the proposed rule would generate arise because providers of the prescribing information would no longer have to print the paper form. The remaining printing would be done by individual users of the prescribing information, who would only print on an as-needed basis. The large range of the estimated impact of the rule reflects not only the uncertainty around some of the estimates but also the large number of entities affected: From 1,450 to 2,000 firms providing prescribing information and 150,000 to 200,000 SKUs needing new labels on the immediate container within 2 years of a final rule. A large number of potential users of prescribing information would also be affected by the proposed rule, including about 66,000 retail and hospital pharmacies and about 380,000 physicians who prescribe drugs. With such a large cohort, even small differences in estimates can create large differences in the totals. Electronic distribution of prescribing information would be new to all parties, and it is difficult to predict how pharmacists, physicians, and other users would react over time or to predict what new technologies may develop as a result of the change. Users would become more familiar with reading on screen and may not need to print prescribing information as often. In addition, new technological solutions may develop over time to simplify access to the prescribing information. ERG did not, however, attempt to adjust cost estimates for these factors.

W. Analysis of Alternatives

We assessed an alternative implementation plan where the implementation date for electronic distribution of prescribing information would be 2 years after the publication of a final rule rather than allowing those firms that had met all the requirements to begin distributing products after the 6-month effective date as proposed.

To calculate the cost difference between the proposal and the alternatives, we assumed that all of the one-time costs would be incurred in the year prior to the proposed implementation

(i.e., the one-time costs would be incurred in year 2 of a 2-year implementation period and the recurring costs and benefits would begin in year 3). The annualized costs of the alternative are presented in table 20. Because most of the costs and benefits are annual costs, which do not change when calculating an annualized effect, there is little difference between the reported values for the two alternatives using this method. The major difference between the two alternatives would be when providers of the prescribing information begin to receive the benefits and users of the prescribing information begin incurring annual costs.

Table 20.--Annualized Costs and Cost Savings of Alternative Implementation Periods ($ millions)

	7% discount		3% discount	
	Low	High	Low	High
2-Year implementation (proposed)				
Total cost savings	$59.3	$147.4	$64.4	$156.0
Costs	-$46.8	-$89.2	-$46.6	-$88.7
Savings – costs	$12.5	$58.2	$17.9	$67.4
3-Year implementation (alternative)	Low estimate	High estimate	Low estimate	High estimate
Total cost savings	$61.2	$150.6	$66.0	$157.2
Costs	-$46.7	-$89.0	-$46.5	-$88.6
Savings – costs	$14.5	$61.6	$19.5	$68.6
Difference between 3- and 2-year implementation	$2.0	$3.4	$1.6	$1.2

X. Regulatory Flexibility Act Analysis

The Regulatory Flexibility Act requires Agencies to prepare a regulatory flexibility analysis if a rule is expected to have a significant economic impact on a substantial number of small entities. The discussion in this section and the previous sections of this document constitute the initial regulatory flexibility analysis.

The Small Business Administration (SBA) defines small entities differently for the different sectors of the economy that would be affected by this proposed rule. SBA defines a biological product manufacturer as small if there are fewer than 500 employees. Drug

manufacturers are small if they employ fewer than 750 employees. Repackers and relabelers are considered drug manufacturers under the FD&C Act. SBA uses sales receipts to define small entities in retail sectors. The definitions for sectors covered by the proposed rule are listed in table 21 and vary from receipts of less than $10 million for physician offices and manufacturers of blood and blood components products up to $34 million for general and surgical hospitals.

We used data from the U.S. Census Bureau to determine the percent of small businesses that would be affected by the proposed rule. The Census collects detailed data by employment size and sales on an establishment basis for the Economic Census. Because Census data are collected by establishment rather than by firm, the percentage of firms reported in table 21 that would be considered small is overstated, but it is clear that with the exception of hospitals and supercenters, most of the firms affected would be considered small. Table 21 shows that the proposed rule would affect a substantial number of small entities.

Table 21.--Definitions of a Small Businesses Affected by Proposed Rule

North American Industry Classification System (NAICS) Code	NAICS Definition	No. of Establishments[1]	2009 SBA Definition of a Small Entity	Percent of Establishments That Are Small
325412	Pharmaceutical preparations and manufacturing	991	Fewer than 750 employees[2]	92%
325414	Biological products (except diagnostic manufacturing)	350	Fewer than 500 employees	96%
446110	Pharmacies and drug stores	39,533	Less than $7 million in sales[3]	99%
445110	Supermarkets and other grocery (except convenience) stores	55,926	Less than $27 million[4]	90%
452910	Warehouse clubs and supercenters	4,196	Less than $27 million[4]	4%
622110	General medical and surgical hospitals	5,052	Less than $34.5 million[5]	11%
621111	Offices of physicians	185,591	Less than $10 million	98%
621991	Blood and organ banks	1,195	Less than $10 million	85%

[1]Source: U.S. Census Bureau, 2002 Economic Census, data obtained via American FactFinder.
[2] Percent based on 500 employees; the 2002 Economic Census does not report data for 750 employees.
[3] Percent based on $5 million; the 2002 Economic Census does not report data for sales of $7 million.
[4] Percent based on $25 million; the 2002 Economic Census does not report data for sales of $27 million; numbers are for all establishments--not just those with pharmacies.
[5] Percent based on $10 million; the 2002 Economic Census greater than $10 million was the highest category identified.

Prescribing information providers (excluding blood manufacturers) would realize net savings from the proposed rule, but the impact would vary greatly by the number of products and SKUs a firm produces and the volume of prescribing information that each firm prints annually. Small entities in these sectors would benefit, but the greater the numbers of products and sales, the greater would be the one-time costs and the annual savings.

The costs of the proposed rule would fall on potential users of the prescribing information. These costs, as described in detail in previous sections of this document and summarized in tables 12 through 17, include additional hardware, training, Internet access, printing, and access and printing time. Table 17 shows the average costs per user establishment; most of the affected establishments are small entities (see table 21). The costs could be over

$1,000 per establishment for small pharmacies and almost $2,700 per establishment for hospital users. These costs would vary by an establishment's sales volume because there would presumably be greater numbers of prescriptions written and dispensed. Individual health care professionals' overall experience and comfort with electronic media would also influence the cost per establishment of this proposed rule.

Manufacturers of blood and blood component products, most of which are small entities, would also incur a net cost as a result of the proposed rule. Unlike pharmaceutical drug products, the prescribing information for blood and blood component products does not have to accompany every container in a shipment; it would take many years before the accumulated savings from no longer providing the prescribing information in paper form surpassed the one-time cost to change all the container labels.

As discussed in the previous section, there is little difference in costs of delaying the implementation of the final rule for users of the prescribing information. It would also not be feasible to operate a dual system allowing some users to continue receiving the paper form of the prescribing information for a longer period of time. Finally, because most users are small entities, exempting or delaying the compliance date of the final rule for small entities would in effect negate the final rule.

In addition to entities covered by the proposed rule, entities who currently supply paper and printing services will see a decline in their business. Many of these entities are small businesses.

Because of the large uncertainty in estimates and lack of information to project how users of the prescribing information will respond to the proposed change, we request comments on the estimates, assumptions, and methodology used in this analysis.

Reference:

R1. Electronic Distribution of Labeling Proposed Rule Final Report Economic Impact Analysis, Report by Eastern Research Group, Inc., October 4, 2010.