ELECTRONIC DISTRIBUTION OF LABELING PROPOSED RULE

Final Report
Economic Impact Analysis
TASK ORDER 1

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SECTION ONE

EXECUTIVE SUMMARY

In this report, Eastern Research Group, Inc. (ERG) examines the costs and benefits of proposed changes to the labeling requirements for prescription pharmaceutical and biologic products. The Food and Drug Administration (FDA) is considering a change that will direct manufacturers to cease production of the paper form of the prescribing information[1] (PI) now provided and to make available an electronic version of the PI. Manufacturers and repackagers will also be required to modify prescription product labels to provide a website where the PI can be accessed, and a toll free telephone number for the individual to request a paper copy of the PI. The regulation would be intended to direct healthcare providers to the most current information available on pharmaceuticals and to prevent the dissemination of the often outdated information found in the PI.

The draft regulation will impose costs on manufacturers as they transition to the electronic version of the PI and to modify labeling. Some manufacturers and repackagers will also incur costs under the proposed rule because of the provision that labeling will have to be submitted to FDA in Structured Product Labeling (SPL) format within six months of the date the final rule is published. These costs will be more than offset by the cost savings manufacturers and pharmaceutical repackagers from no longer having to print and affix the paper PI to their packaging. Pharmacists will have to adjust their practices from relying on paper copies of the PI to accessing the same information electronically. The significance of this change for pharmacists will vary with the degree of their reliance on the paper version of the PI (which is in many cases quite low) and upon their access to the Internet. Some pharmacies, particularly chain pharmacies, do not provide the staff with Internet access.

Table 1-1 presents a summary of annualized costs and cost savings estimated for the draft regulation under various compliance timelines. Total annualized costs are the sum of recurring annual costs and annualized one-time costs, the latter of which are annualized over ten years at either a three or seven percent discount rate. Under the baseline scenario (requiring submission of labeling within six months and provision of electronic PI within two years), annualized costs will be between $75.5 million and $148.8 million at a 3 percent discount rate and between $80.8 million and $157.8 million at a 7 percent discount rate. Cost savings are all recurring annual costs and there are no one-time costs to annualize. Overall, the draft regulation generates large cost savings. Large cost savings are also anticipated for the elimination of the paper PI, with cost savings of between $93.8 million and $216.5 million. The bulk of the costs will be borne by pharmacists and other users of PI, while the bulk of cost savings will be realized by manufacturers and repackagers.

FDA is also exploring an alternative regulatory approach that would alter the timeline for compliance. As a baseline in estimating costs, ERG assumed that all labels will be required to be submitted to FDA in SPL format within six months after the final rule is published and that electronic PI will be required within two years. As alternatives, ERG considered scenarios where labels are not required to be submitted to FDA in SPL format for two years after the final rule is published, and where the switch from paper labeling to electronic labeling occurs either one year or three years after the final rule is published. Increasing the timeline for submitting labeling in SPL from six months to two years after the final rule is published would decrease costs, although the difference accounts for less than two tenths of a percent of total costs. Reducing the timeline within which PI is required to be in electronic form from two years to one year would increase costs for manufacturers and repackagers by approximately 7 to 8 percent. Based on our approach to estimating labeling costs, there are no changes in costs as a result of extending the compliance timeline from two years to three years.

[1] In this document the term “prescribing information” refers to information directed at pharmacists and healthcare providers rather than that directed at patients, unless otherwise noted. Information directed at patients is part of the PI as well, but is not affected by the current regulation.

The proposed regulation has the potential to improve health outcomes by ensuring that pharmacists and health care practitioners have ready access to the most up-to-date version of pharmaceutical and biologic labeling information. Today, the PI is only current through the time when it is printed, and may lack important, more recent, safety information. “Dear Doctor” or “Dear Health Care Professional” letters help to address this problem, but these are sometimes unclear or go unnoticed by the healthcare provider.Electronic PI should help alleviate these problems. Preliminary evaluations of pilot systems that provided electronic PI to pharmacists also suggest that it may be referred to more frequently than paper PI.

Table 1-1. Total Annualized Cost Savings and Costs of the Proposed Regulation

Cost Savings	**Low Estimate**		**High Estimate**	
Manufacturers	$20,988,420		$52,628,980	
Repackagers	$72,766,500		$163,912,500	
Total Cost Savings	**$93,754,920**		**$216,541,480**	
Costs	**3% Discount Rate**		**7% Discount Rate**	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**
1 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$9,732,785	$23,108,739	$11,373,049	$26,411,078
Repackagers	$22,750,366	$46,168,345	$26,780,465	$52,884,669
Total Costs (without SPL costs)	$78,739,350	$157,533,527	$84,591,132	$168,022,873
Total Costs (with 6 month SPL implementation)	**$80,274,757**	**$159,466,949**	**$86,455,898**	**$170,371,032**
Total Costs (with 2 years SPL implementation)	**$80,100,527**	**$159,247,554**	**$86,244,293**	**$170,104,574**
2 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$8,531,861	$20,173,157	$9,954,736	$22,994,603
Repackagers	$19,169,383	$38,389,655	$22,508,552	$43,726,967
Total Costs (without SPL costs)	$73,957,443	$146,819,255	$78,900,907	$155,448,696
Total Costs (with 6 month SPL implementation)	**$75,492,850**	**$148,752,677**	**$80,765,672**	**$157,796,855**
Total Costs (with 2 years SPL implementation)	**$75,318,619**	**$148,533,282**	**$80,554,068**	**$157,530,397**
3 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$8,531,861	$20,173,157	$9,954,736	$22,994,603
Repackagers	$19,169,383	$38,389,655	$22,508,552	$43,726,967
Total Costs (without SPL costs)	$73,957,443	$146,819,255	$78,900,907	$155,448,696
Total Costs (with 6 month SPL implementation)	**$75,492,850**	**$148,752,677**	**$80,765,672**	**$157,796,855**
Total Costs (with 2 years SPL implementation)	**$75,318,619**	**$148,533,282**	**$80,554,068**	**$157,530,397**

SECTION TWO

PROFILE OF AFFECTED INDUSTRIES

The proposed regulation to make prescribing information contained in PI electronic will affect several industries, including pharmaceutical and biologics manufacturers, pharmacies, clinics, health care plans, hospitals, nursing homes, physicians' offices, home health care services, pharmaceutical printers, and the paper manufacturers who supply those printers. This section presents basic information on the size and composition of those industries.

Table 2-1. Affected Entities

Type of Entity	Number	Source
Pharmaceutical Manufacturers		
Brand manufacturers		
Low estimate - small/medium	163	ERG, 2008; FDA estimate
High estimate - small/medium	207	ERG, 2008; FDA estimate
Low estimate - large (500 employees or more)	156	ERG, 2008; FDA estimate
High estimate - large (500 employees or more)	198	ERG, 2008; FDA estimate
Generic manufacturers		
Low estimate	232	ERG, 2008; FDA estimate
High estimate	295	ERG, 2008; FDA estimate
Total manufacturers - low estimate	550	
Total manufacturers - high estimate	700	
Repackagers/Relabelers		
Low estimate	900	FDA estimate
High estimate	1,300	FDA estimate
Pharmacies		
Number of chain store headquarters	244	HDMA, 2008; 25% of drug and grocery stores
Total Chain (sum of drugstore, supermarket, mass merchant) [a]	38,695	NACDS, 2007
Chain drugstore (at least 4 stores)	22,013	NACDS, 2007
Supermarket (food, convenience, grocery store)	9,300	NACDS, 2007
Mass merchant (mass merchandise/discount store)	7,382	NACDS, 2007
Independent (one to three stores) [a]	16,921	NACDS, 2007
Hospital outlets (all accounts at the address of hospital) [a]	10,362	HDMA, 2008
Nursing home/home health/long term care [a]	4,514	HDMA, 2008
Healthcare plan [a]	1,058	HDMA, 2008
Mail order [a]	259	HDMA, 2008
Miscellaneous institutions [a][b]	7,153	HDMA, 2008
Prescribing Physicians using PI		
	377,123	COGME, 2005; BLS, 2007f

Table 2-1. Affected Entities

Type of Entity	Number	Source
PI Printers		
	45	Paper Manufacturer A (2009); Printer C (2009)
Paper Suppliers		
	3	Paper Manufacturer A (2009); Printer C (2009)

[a] Based on IMS Health Trade Data Classifications.

[b] These include jails and prisons, colleges/universities without a hospital, industrial medical departments, fire and police departments. They were included in the HDMA Factbook under miscellaneous, along with animal hospitals and pharmaceutical manufacturers and drug warehouses not reporting sell-out to Drug Distribution Data (IMS Health).

2.1 PHARMACEUTICAL AND BIOLOGICS MANUFACTURERS

FDA's analysis of its Approved Drug Products with Therapeutic Equivalence Evaluations, National Drug Code (NDC), and Establishment Registration and Device Listing databases suggests a total of between 550 and 700 unique manufacturing firms. In order to categorize these firms by size and whether they manufacture brand or generic products, we applied ERG's (2008) distribution of unique companies filing New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), Biologics License Applications (BLAs), or efficacy supplement submissions with FDA between 2002 and 2006. This distribution categorizes the manufacturers by type: small and medium brand manufacturers, large brand manufacturers, and generic manufacturers (ERG's conversations with industry experts suggested that small and medium brand manufacturers have similar manufacturing processes and costs). In this analysis, small and medium firms (those with fewer than 500 employees) accounted for 30 percent of all manufacturers, large firms (with more than 500 employees) accounted for 28 percent, and firms manufacturing generic products accounted for 42 percent (see Table 2-2).

Table 2-2. ERG (2008) and FDA Supplied Counts of Distinct Firms Making Submissions by Category

ERG, 2008			FDA	
Type of Entity	**Number**	**% of Total**	**Low Est.**	**High Est.**
Small/medium brand	144	30%	NE	NE
Large brand	138	28%	NE	NE
Generic	205	42%	NE	NE
Total	**487**	**100%**	**550**	**700**

NE = Not Estimated

Applying these percentages to FDA's estimate of the total number of manufacturers suggests that there are between 163 and 207 small/medium manufacturers, between 156 and 198 large manufacturers, and between 232 and 295 generic manufacturers, summing to a total of between 550 and 700 manufacturers (see Table 2-3).

Table 2-3. Number of Pharmaceutical and Biologics Manufacturing Firms by Category

Type of Entity	Number
Pharmaceutical Manufacturers	
Brand manufacturers	
Low estimate - small/medium	163
High estimate - small/medium	207
Low estimate- large (500 employees or more)	156
High estimate - large (500 employees or more)	198
Generic manufacturers	
Low estimate	232
High estimate	295
Total manufacturers - low estimate	**550**
Total manufacturers - high estimate	**700**

2.2 REPACKAGERS, RELABELERS, AND DISTRIBUTORS

We derived our estimate of the number of repackagers (defined as relabelers, repackagers, and private label distributors[2]) from an analysis by FDA of its NDC and Establishment Registration and Device Listing Databases. FDA supplied estimates suggest that there are between 900 and 1,300 repackagers, relabelers, and distributors affected by the rule based on the number of these firms that list unique NDC numbers.

This estimate is much larger than any estimates we could develop independently from published or Internet sources, such as Thomas Register or Thomasnet, or from industry trade associations. The FDA estimate captures a number of entities that would not appear in published sources as repackagers, relabelers or distributors because they meet the regulatory definition but do not necessarily offer their services to third parties. They will be affected by the regulatory changes because they have unique NDCs and are required to publish their own labeling.

2.3 RETAIL PHARMACIES

There are approximately 55,875 retail pharmacy establishments in the United States. Within retail pharmacies, there are several sub-types of pharmacies (HDMA, 2008):

- Chain pharmacy: A store that fills prescriptions and is part of a group of at least four stores
- Food Store with Pharmacy: Includes food, convenience, grocery, and supermarket stores with pharmacies
- Independent Pharmacy: A store that fills prescriptions but is not part of a chain; may be a one to three store combination

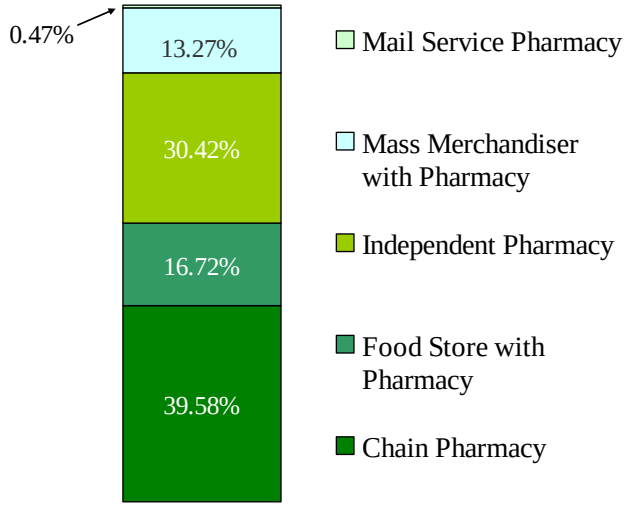
[2] The contracted manufacturers or packagers for private label distributors will actually be incurring the costs and savings from the proposed rule. They would presumably reflect the impacts in the prices they charge for their services. However, to capture the costs and savings per SKU using FDA's current listing data, the individual SKUs were counted using a private label distributor code.

- Mail Service Pharmacy: A facility that fills prescriptions by mail, which includes Internet pharmacies, including mail service pharmacies operated by managed cared organizations

- Mass Merchandiser with Pharmacy: Includes any mass merchandise/discount store with a pharmacy

There are 22,013 traditional chain pharmacy establishments comprising 40 percent of pharmacies, 9,300 food store pharmacy establishments (17 percent), 16,921 independent pharmacy establishments (30 percent), and 7,382 mass merchant chain pharmacies (13 percent) (NACDS, 2007).

Estimates of the number of mail order/Internet pharmacies vary. Oliver (2001) estimated that there were 400 pharmacies doing business over the Internet, which would compose less than one percent of all pharmacy establishments. The National Association of Boards of Pharmacy (NABP, 2009) lists 16 recommended online pharmacy companies, which together are associated with 60 dispensing pharmacies, which would be less than a tenth of one percent of all pharmacies. The Healthcare Distribution Management Organization (2008) estimated that in 2007 there were 259 mail service and Internet pharmacies, composing less than half a percent of all retail pharmacies, and this is the estimate we use in our analysis.



Source: NACDS (2007); HDMA (2008)

Figure 2-1. Types of Retail Pharmacies

Pharmacy staff members include pharmacists, pharmacy technicians, and pharmacy aides. Pharmacists (who dispense medication and counsel patients) are most likely to refer to PI, while pharmacy technicians (who prepare prescribed medication) and pharmacy aides (whose duties are more administrative) may be less likely to do so (BLS, 2009).

2.4 CLINICS

Clinics, as defined by the Healthcare Distribution Management Association (HDMA, 2008) are physicians or groups of physicians located at the same address offering services such as family planning, x-rays, dialysis, oncology, emergency treatment, and alcohol/drug treatment. HDMA (2008) estimates that there are approximately 71,219 clinics in the United States. Nevertheless, ERG believes that

including both HDMA's estimate and U.S. Department of Health and Human Services' Council on Graduate Medical Education's (2005) count of physicians (see section 2.9 below) would result in double counting, and thus we do not include a separate category for clinics.

2.5 HEALTH CARE PLANS

Health care plans include staff-model health maintenance organizations that have in-house pharmacies, such as hospitals, pharmacies, clinics, and warehouses, as well as worker's compensation and union shop clinics/pharmacies (HDMA, 2008). The HMDA (2008) estimates that there are 1,058 of these entities.

2.6 HOSPITALS & HOSPITAL PHARMACIES

The American Hospital Association (AHA, 2007) estimates that there were 5,708 hospitals in the United States, including community hospitals, government hospitals, psychiatric facilities, and long term care facilities. The HDMA (2008) estimates that there are 10,362 hospital outlets. This definition includes all accounts at the address of the hospital, such as pharmacies, dispensaries, departments, physicians, outpatient clinics, Veterans Administration facilities, military facilities, and U.S. public health accounts. ERG uses the HDMA estimate for purposes of our cost analysis, as the AHA (2007) estimate fails to account for the multiple sites within each hospital that may be affected by the proposed regulation.

2.7 INFUSION CENTERS

Infusion centers, where patients receive drugs intravenously, have several delivery models. These include hospital-based services, emergency departments, outpatient infusion clinics, visiting nurses, home infusion companies, and long term care facilities (Hankins, 2001). For purposes of our analysis, we assume that infusion centers of these various types are included among other groupings, such as hospitals and clinics.

2.8 NURSING HOMES

THE HMDA (2008) defines nursing homes as residential care facilities not located at a hospital. These include traditional nursing homes, rest homes, convalescent centers, nursing home providers, visiting nurses, and home healthcare providers. The HMDA (2008) estimates that there are 4,514 of these entities that purchase prescription drugs.

2.9 PHYSICIANS

In estimating the number of physicians who use PI, ERG began with COGME's (2005) projection that there will be 899,540 active physicians in the U.S.in 2010. ERG reduced this number by COGME's (2005) estimate regarding the number of physicians who are not active in patient care (6 percent). Those physicians who are active in patient care include surgeons, who are not expected to consult PI. BLS (2007f) estimates that 10.8 percent are in surgical specialties and so ERG further reduced the number of active physicians by that amount to obtain the number of prescribing physicians. ERG further assumes that approximately half of these physicians would not typically refer to PI, whether because they routinely prescribe the same drugs or because they use other sources of drug information. This leaves 377,123 physicians who ERG estimates would make some use of the PI.

2.10 OTHER INSTITUTIONS

Other institutions that might administer prescription drugs, including prisons, jails, fire departments, police departments, veterinarians, and colleges/universities without a hospital, total 7,153 entities (HDMA, 2008). Based on a 2005 Census of State and Federal Correctional Facilities, there are 1,821 state and federal correctional facilities (U.S. Department of Justice, 2008a). Furthermore, based on data from 1999 Census of Jails and the 2005 Census of Jail Inmates, there are also 2,876 local jails (U.S. Department of Justice, 2008b). It is not clear that all jails and prisons have pharmacies, however, so these numbers may overstate the total number of jails and prisons in the count of 7,153 miscellaneous institutions. For the same reason, ERG cannot isolate counts of the other groups, such as fire and police departments. In the absence of more data and as a conservative estimate, ERG used the entire count of 7,153 miscellaneous institutions (which also includes some veterinarians not affected by the rule but cannot be separated out) to estimate costs in section 6.0.

2.11 PHARMACEUTICAL PRINTERS

Based on ERG's conversations with industry experts, we estimate that there are approximately 40 to 50 printers dedicated to pharmaceutical printing, some of which operate multiple plants (see section 3.1.4 for more details).

2.12 PAPER SUPPLIERS

Based on ERG's conversations with industry experts, we believe that there are three paper manufacturers who supply the paper used for PI to pharmaceutical printers, and that between 30 and 80 percent of their lightweight paper manufacturing is dedicated to pharmaceutical printing (see section 3.1.5 for more details).

SECTION THREE

BASELINE TRENDS

3.1 CURRENT PRACTICES OF MANUFACTURERS WITH RESPECT TO PI

3.1.1 The PI in Paper Form

Currently, manufacturers provide a paper version of the professional PI directed at pharmacists and healthcare providers for every prescription drug manufactured, and sometimes provide patient prescribing information as well. One paper version of PI is provided per container, regardless of container size, and they are usually attached to the container or inserted into the carton, if a carton encloses the container.

The Pharmaceutical Research and Manufacturers of America (PhRMA) released a white paper in 1999 entitled "Distribution of Product Information to the Product Dispensing Site Electronically: The Case for Elimination of the Paper PI." The paper outlines the manufacturing steps in creating the PI in paper form. While potentially dated by the most recent developments in manufacturing efficiencies, the principal aspects of the process remain unchanged. The steps described in the PhRMA white paper are as follows:

1) Content and format is finalized either within the company or after consultation with the FDA. Final approval by the FDA (depending on type of change).

2) If initial PI for a new product is produced, the text is generally converted from a word processing file.

    a) Type is set.

    b) Proofs are printed.

    c) Proofs are read, approved and returned to printer.

    d) PI is printed.

    e) PI is folded.

    f) PI is warehoused until needed on the manufacturing line.

    g) PI is attached or inserted to product bottles or containers.

3) Various controls and checks are in place at each step of these processes to assure PI is accurate and attached to the appropriate product.

These steps take a few weeks to complete. Costs include regulatory review, label creation, label printing, paper costs, folding and attaching or inserting the PI, inventory loss, and quality assurance. Many manufacturers outsource printing of the PI, including the quality control, and storage, while others still review the insert for quality assurance and store the PI on-site (Expert A, 2009; Packager A, 2009).

Paper forms of PI usually have very small font sizes and are printed on very large sheets. A Genentech executive commented before FDA's panel for the public hearing on "Electronic Distribution of Package Inserts for Prescription Drug Products" (held April 27, 2007) that several of her company's

inserts have gotten so large due to increased indications and other information that some cover a small picnic table. Some prescription drug cartons are larger due to paper PI, which adds costs for manufacturing, transportation, and storage, including cold storage. Pharmacies, including those at hospitals, must maintain significantly more storage space for some products (Foxhall, 2007).

The PI is frequently revised to reflect new safety data or to comply with new regulations. One manufacturer noted that updates of the PI for some drugs can occur as frequently as 2 to 3 times a year, or more (Manufacturer A, 2009). New products will experience more frequent labeling changes than established and generic products (Expert A, 2009). The information in the paper PI might be outdated if the product is not manufactured frequently. For example, the PI of products manufactured once a year might be over a year old before the product reaches the pharmacy (PhRMA, 1999).

Experts and industry contacts have estimated that the average cost ranges from $0.04 to $0.06 per copy of the PI (Expert A, 2009; Printer A, 2009; Printer B, 2009). Manufacturers have also reported that the production of package inserts is very costly to industry. Brand name manufacturers spend anywhere from $3 to $5 million each annually on the production of PI (Conlon, 2001), although no detail was provided for this estimate. A survey conducted by the Generic Pharmaceutical Association of its members regarding the cost of PI labeling resulted in similar estimates of $2 to $3 million annually for a midsize to large manufacturer (GPhA, 2007). This estimate includes labor, printing, storage, and destruction costs (GPhA, 2009).

3.1.2 Medication Guides and Patient Package Inserts (PPI)

Medication Guides and PPIs are considered part of the PI (although they are not affected by the current regulation). For certain drugs, manufacturers are also required by FDA to provide information for the patient in the form of patient labeling such as Medication Guides or other PPI. Currently, most of these are provided to the pharmacies in paper form with each drug affected by the requirement. Medication Guides contain critical drug information on safety risks specifically related to the drug and are intended to be given to each patient when the patient receives the drug from the pharmacy. Medication Guides should be provided to each pharmacy in sufficient quantities to accommodate the number of prescriptions the pharmacy expects to fill for that drug, or the manufacturer should provide the pharmacies with the means to produce medication guides in sufficient numbers. Manufacturers would consider making these available to pharmacies electronically too, if allowed (Manufacturer B, 2009a).

PPIs are currently required to be provided in paper form and dispensed with certain drugs, such as oral contraceptives and estrogen therapies. NDA and BLA applicants will sometimes request a PPI for a particular product to provide patients with specific information for proper use. These PPIs are FDA approved and become part of the official labeling (Manufacturer B, 2009a). In a separate analysis, ERG found that approximately half of the drugs with PPI are distributed in unit-of use packaging.

Manufacturers of approved products are required to submit Medication Guides and other PPI electronically using SPL. SPL is a Health Level Seven, Inc. standard for the exchange of product information using extensible markup language (XML). Other medication information that a patient might receive such as patient information produced by third party information vendors is not part of FDA approved labeling and is not submitted to FDA (FDA, 2005).

3.1.3 Current Electronic Requirements for PI

All drug manufacturers of approved products should have complied by now with the requirement to submit PI to FDA in a standard electronic format. In the Federal Register of December 11, 2003 (68 FR 69009), FDA issued a final rule to require submission of the content of labeling required under 21 CFR

201.100(d)(3) for human prescription drugs and biological products in an electronic format. At that time, the PDF format was acceptable. However, section 224 of the Food and Drug Administration Amendments Act of 2007, which amends section 510(p) of the Act, expressly requires drug listing information to be submitted by electronic means by June 1, 2009. This provision extends the requirement for electronically submitting labeling in SPL format to contract manufacturers, repackagers, and relabelers. However because this is a listing requirement, the firms do not have to submit the label in SPL until the PI currently listed is revised (FDA, 2009). The new electronic labeling is a key element of and primary source of medication information for DailyMed, an interagency online health information clearinghouse created cooperatively by FDA and the National Library of Medicine (NLM). As of September 14, 2009, DailyMed included 4,981 approved prescription products but it does not yet contain a complete listing of approved products (either brand or generic) (NLM, 2009).

Most brand name pharmaceutical manufacturers also have an electronic version of the PI on their Web site (Manufacturer B, 2009b). In these cases, a Google search using the text "prescribing information" and the name of the product often brings up the PI in PDF format.

In some cases, a manufacturer may only post the PI for the most recent version of a drug, even if earlier versions of the drug are still being dispensed. In that case, the only source for the older drug's PI is the paper version that accompanied the drug (Pharmacist A et al., 2009).

3.1.4 Pharmaceutical Printers

As noted above, pharmaceutical manufacturers outsource most of their pharmaceutical literature production to outside printers. Pharmaceutical printers produce some or all forms of pharmaceutical literature: labels, professional PI, PPIs (including Medication Guides), and cartons. Approximately 40-50 printers in the U.S. can be considered dedicated to pharmaceutical printing, based on their investments in machines that produce lightweight, miniature literature with multiple folds. Some printing companies operate multiple plants (Paper Manufacturer B, 2009; Paper Manufacturer A, 2009).

There are two types of printing machines, sheet-fed and web. The sheet-fed machine uses discrete sheets of paper and can be used for other printing processes. The web machine uses a continuous roll of paper and has limitations that prevent it from being used for most other printing tasks. Web machines do not allow color printing and lack an energy source for heating ink or dryers to set inks. However, the profit margin for printing using sheet-fed machines is lower than web machines, and the market for sheet-fed printing currently has excess capacity (Paper Manufacturer A, 2009).

Printers dedicated to pharmaceutical printing are differentiated by their use of specialized folding machines. Folders represent the biggest equipment expense for pharmaceutical printers, and can cost from $100,000 to $750,000, depending on the complexity of the machine. The number of folders per printer varies from one or two to as many as two dozen (Paper Manufacturer B, 2009; Paper Manufacturer A, 2009). The degree to which literature needs to be folded depends in part on FDA requirements for PI content and minimum font size. When more information is required, the insert must be printed on lighter weight paper and folded more times to be attached to or inserted alongside a drug container. As paper PI gets larger, printers need to add components to the machine to increase the number of folds. Medication Guides and other PPI are also produced using miniature folding machines (Paper Manufacturer B, 2009).

Pharmaceutical printers can outsource some of their folding work to trade binderies when they do not have enough in-house capacity. Trade binderies only operate folding equipment, and take in work from other industries, such as from card and envelope producers (Paper Manufacturer B, 2009).

Pharmaceutical printers expressed concern about the loss of business if electronic distribution of the PI were to become standard. The printers stated that they are at a productivity disadvantage compared to other commercial printers because their machines and quality control processes are specialized to meet needs of pharmaceutical industry (Paper Manufacturer B, 2009). They also noted that their folding machines cannot be used elsewhere because very few industries require miniature folding on lightweight paper (Paper Manufacturer A, 2009; Paper Manufacturer B, 2009).

ERG is aware of two brand name pharmaceutical manufacturers (Merck and Covidien) and one generic manufacturer that print the PI in-house, and industry contacts also confirmed that printing by manufacturers represents only a small percentage of pharmaceutical printing (Expert A, 2009; Paper Manufacturer B, 2009; Manufacturer E, 2009).

3.1.5 Paper Suppliers to Pharmaceutical Printers

Three paper companies produce the majority of the thin, lightweight paper used for paper PI in the United States: Fraser Paper, Boise, and Domtar. Fraser Paper and Domtar are Canadian-owned companies that operate mills in the U.S. Some debate exists about what percentage of thin-paper production is accounted for by pharmaceutical literature. One industry source contacted by ERG estimated that, of the 250-350 million tons of free sheet paper produced in the U.S., 40 million tons is used to print pharmaceutical literature (Paper Manufacturer B, 2009). Another reported that 30 percent of thin paper production is used for pharmaceutical printing (Paper Manufacturer A, 2009). Thin paper is also used to produce cosmetic inserts, bibles, financial and congressional reports, and telephone directories (Paper Manufacturer B, 2009).

Considering only the thin paper used in the pharmaceutical industry, approximately 50 percent is used to print paper copies of the professional PI and the other half is used for PPI, Medication Guides, and other types of inserts. PI content might also be printed on non-lightweight paper if it is not to be distributed as inserts but rather with drug representative marketing brochures or other materials (Paper Manufacturer B, 2009).

3.1.6 Repackagers, Relabelers and Distributors

Many pharmaceutical manufacturers outsource at least some of their packaging activities to contract pharmaceutical packagers. A 2000 study found that 85 percent of pharmaceutical manufacturers contracted out primary packaging (the immediate container for the drug), and 78 percent contracted out secondary packaging (such as cartons) (Lubinsky, 2000). Contract packagers receive drugs from the manufacturers in bulk and package them into units for sale to pharmacies. Packagers provide the final content of the PI to third-party pharmaceutical printers for production, and then receive the complete, pre-folded inserts. Packagers include the paper PI in cartons when each container is packaged in an individual carton, or attach the insert to the drug container. Containers can be bundled together with shrink-wrap, which protects the attached PI from accidental removal (Packager A, 2009).

Pharmaceutical packagers typically perform two steps when they receive paper PI from pharmaceutical printers (Expert A, 2009). Many manufacturers, especially large companies, do this electronically. First, samples of the insert are scanned and compared using software designed to identify small differences between the manufacturer's version of the PI and the version received from the printer. After, when the insert is attached or included with the drug container, a barcode reader on the packaging line scans the barcode printed on each insert to determine that it reflects the final, FDA-approved version of the insert and that each package contains an insert (Packager A, 2009; Wilson, 2009; Wong, 2009).

Pharmaceutical repackagers purchase a finished product from a manufacturer, remove drugs from the manufacturers' packaging and repackage them in different, generally smaller containers. Repackagers must produce the PI for the drugs they repackage to reflect their role in the processing of the drugs and like the original manufacturer must ensure the PI accompanies their containers. Repackagers also create the labels for the drug containers they produce (Distributor A, 2009; Distributor B, 2009).

Some pharmaceutical repackagers also produce kits that may contain multiple drugs or drugs and medical devices. Kits are produced for a range of medical needs, including surgery. Kits currently include a paper PI for each medication in the kit (Repackager A, 2009).

Wholesale distributors purchase drugs from drug manufacturers or repackagers to sell to pharmacies and other pharmaceutical dispensers. If a distributor needs additional copies of the PI in order to sell one unit of a multi-unit package, it must order the copies from the manufacturer. These cost roughly $0.40 to $0.50 per copy (Distributor A, 2009).

Repackagers, packagers, and wholesale distributors typically use automated picking systems (APS) to transfer drug containers from storage shelves to each customer's shipment. When the PI has already been inserted inside a box alongside the drug container, then the PI does not affect distributors' processes. If the PI is attached to the outside of a drug container and the drug container is not in a box or in a shrink-wrapped multi-container package, the paper PI can interfere with the automated transfer from shelf to shipment. The containers must first be aligned so that the attached PI is in the same location on each container, which minimizes the risk that the PI will detach from the container or that the PI will cause the automated picker to malfunction. Each day between 1,600 and 3,550 copies of the PI become loose and fall into the automated picking system (Repackager B, 2009). Malfunctions due to paper PI do not occur on a daily basis, but do occur regularly. Each malfunction requires about 3 minutes of down time and distributors must spend time finding and reattaching PI that becomes detached from drug containers. (Distributor B, 2009). One repackager estimated that errors caused by paper copies of the PI result in costs of between $1,372 and $5,705 per month at each repackaging site, which includes the labor costs and the cost of replacing damaged machine parts (Repackager B, 2009).

3.2 CURRENT METHODS OF ACCESSING PRESCRIBING INFORMATION BY PHARMACISTS

The way drug information is accessed may vary somewhat by state (due to varying state Board of Pharmacy regulations) and by facility. Nevertheless, there are some commonalities in our discussions on professional PI use by pharmacists, as outlined here.

3.2.1 Pharmacists

Pharmacists share common workflow patterns when dispensing drugs, regardless of the type of pharmacy in which they work. The dispensing activity starts when the pharmacist receives a new prescription or refill request for a patient. This request is processed on a computer through one of many types of dispensing software available to pharmacies.

The pharmacist first determines that the prescription is appropriate for the patient. This may involve checking current patient medication use and reference material for guidance on dosage, interactions, and special patient conditions, such as pregnancy or breastfeeding. Pharmacists might refer to the paper PI for this information, but are also likely to consult a paper or electronic compendium such as Facts and Comparisons, Micromedex (including the Physicians' Desk Reference (PDR)), Up-to-Date, or other regularly updated sources of drug information. Schrimsher et al.'s (2006) survey of 604 pharmacists in Alabama found that Drug Facts and Comparisons was the most used source of drug

information, followed by PDR. The pharmacists that ERG spoke to also reported using electronic sources, as outlined in this section. The electronic sources available are discussed in more detail in section 3.4.2.

Once the pharmacist has confirmed the appropriate dosage and form in which to dispense the drug, the pharmacist determines how to process and prepare the drug. This might involve dispensing the drug into a smaller container, preparing a liquid form of the drug through reconstitution or mixing with water (such as a liquid antibiotic for children), or compounding the drug to create an intravenous solution. Whether the pharmacist is more likely to refer to the paper PI or some other source for information on how to process or prepare the drug and for information on drug interactions or side effect is largely a personal preference (Expert C, 2009; Pharmacist G, 2009).

The current use of paper PI presents some disadvantages to pharmacists, as the paper takes up space on the shelf (up to ¼ inch on the side of each container), which reduces the storage space for drug containers (Pharmacist C, 2009).

3.2.2 Chain Store Pharmacists

For purposes of estimating costs, ERG defines a chain pharmacy as a company with four or more stores, including food stores with pharmacies and mass merchandisers with pharmacies. This group encompasses pharmacists employed at the three largest national drugstore chains, CVS, Walgreens, and Rite-Aid, and at chain supermarkets and retailers such as Albertson's and Target. There are 38,695 stores in this category (NACDS, 2009)

Chain store pharmacists need to refer to paper PI or other information sources less often than pharmacists at hospitals because they generally dispense fewer types of drugs. Compared to a hospital pharmacy, fewer conditions are treated, there are fewer dosage forms, and generally less serious contraindications for drugs dispensed at chain pharmacies. Customers might ask chain store pharmacists to provide them with the paper PI, but the frequency of this, although variable, is relatively rare (Pharmacist Association A, 2009; Pharmacist A et al., 2009).

Pharmacies within a chain are typically connected to an intranet network that serves all of the chain's pharmacies. Drug information software, such as Facts and Comparisons, might be available on a central server and accessed through the intranet (Pharmacist A et al., 2009).

Chain pharmacies are more likely to block or restrict Internet usage than independent retail pharmacies (Pharmacist B, 2009), though some chains have unrestricted access (Pharmacist F, 2009). Those that restrict access might wish to discourage employees from spending time on the Internet at work or have concerns for the security of patient data. Generally, dispensing activities are conducted on a set of dedicated computers while non-dispensing activities, including checking email, are conducted on a separate computer (Pharmacist Association A, 2009).

3.2.3 Independent Pharmacists

Independent pharmacies are defined as being privately owned retail businesses consisting of three or fewer locations. There are 16,921 independent pharmacies (NACDS, 2009), which employ on average 2.6 pharmacists and 3.7 technicians (NCPA, 2008).[3] Based on conversations with chain and independent

[3] NCPA includes owner-operated franchises of national chain pharmacies in their membership, and counts 23,318 independent pharmacies. However, for this analysis, we are including owner-operated franchises in the chain pharmacy category, as these pharmacies' Internet access more closely parallels that of other chain pharmacies. We instead use the National Association of Chain Drug Stores' (NACDS) estimate of independent pharmacies.

pharmacists, ERG judges that pharmacists at independent pharmacies refer to paper PI with a frequency similar to chain store pharmacists.

Thomson Healthcare, a third party information vendor, surveyed pharmacists on their use of PI prior to conducting a large-scale field trial in 2004 of their electronic PI device. They found out that nearly one-half (49.3 percent) of the pharmacists participating in the study consulted the paper PI once or twice a week. Another third (29.3 percent) consulted it once or twice a month. Only nine pharmacists (12 percent) referred to the PI daily. Another seven (9.3 percent) reported that they almost never refer to it. Across all 170 sites surveyed over 4 weeks, the PI was consulted 300 times (Rupp, 2006). This indicates that PI use among independent pharmacists is significant, if not universal.

Pharmacist Association B (2009) estimates that 99 percent of independent pharmacies have access to the Internet. Similar to chain store pharmacies, independent pharmacies typically dedicate one or more computers to prescription dispensing activities, and have at least one computer on-site that is not used for dispensing data that might be used for Internet access. This arrangement protects patient data because the computers used for filling prescriptions are protected behind a firewall (in accordance with HIPPA regulations). The general practice is to allow Internet access only on Internet computers that do not carry patient data (Pharmacist C, 2009; Expert B, 2009). According to estimates of pharmacists contacted, the computer(s) connected to the Internet are not in constant use, and could be used to access manufacturers' Web sites. Some independent pharmacists already seek out PDF versions of PI on manufacturers' Web sites (Pharmacist C, 2009; Pharmacist D, 2009). As in the case of other pharmacies, paper PI takes up room on independent pharmacy shelves.

3.2.4 Health-System and Hospital Pharmacists

For the purpose of estimating costs, the hospital and health-system pharmacies group includes surgery centers, correctional facilities with a pharmacy, and rehabilitation centers (Expert B, 2009). The HDMA (2008) estimates that there are 10,362 pharmacies in these settings.

In a hospital setting, the paper PI arrives with each drug container, but might be removed by the first person to open the container. Thus, it might not be stored next to the container (Pharmacist Association C, 2009). Hospital pharmacists reportedly refer to the paper PI two to five times a week, often for dosing information, to check drug interactions, or for constitution and compounding if injectable products are involved. Pharmacists in a hospital setting might refer to the paper PI more frequently than pharmacists in a retail setting because they might work with a wider range of drugs and might be providing those drugs in a wider range of formats to patients with more varied conditions and drug interaction risks (Pharmacist D, 2009).

Trained pharmacy technicians also refer to PI, particularly during compounding, to create intravenous (IV) solutions. In 2006, U.S. Pharmacopoeia (USP) issued USP 797, which dictates the conditions of "clean rooms" in which sterile solutions may be created and the time for which they may be stored. Because the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has adopted USP 797, all JCAHO-accredited hospitals must adopt USP 797. USP 797 prohibits the use of computers in clean rooms. Therefore, pharmacists and pharmacy technicians wishing to refer to electronic PI while compounding drugs need to print the paper PI before entering the clean room (Expert B, 2009; Pharmacist D, 2009).

Some hospital pharmacists report seeking information from regularly-updated drug information software rather than the paper PI. Douglas Scheckelhoff, director of pharmacy practice sections, American Society for Health-System Pharmacists, testified before an FDA panel for the public hearing on "Electronic Distribution of Package Inserts for Prescription Drug Products" (held April 27, 2007) that for

most routine questions, hospital pharmacists already use reference books or electronic resources (Foxhall, 2007). As in the retail setting, hospital pharmacists make use of electronically distributed sources of drug information, such as Facts and Comparisons, Up-to-Date, and Micromedex, among many others (Pharmacist D, 2009). Schrimscher et al. (2006) found that Personal Digital Assistant (PDA) use was higher among hospital pharmacists than among pharmacists in other types of settings, with 32.4 percent of hospital pharmacists reporting use of a PDA to find drug information (although it was not specified with what frequency).

Some pharmacists work in the hospital wards rather than in the pharmacy. They usually do not have access to paper PI. Instead, they might refer to the downloadable databases of drug information that are available from drug information software providers such as Micromedex (Pharmacist D, 2009).

Similar to pharmacists in independent pharmacies, some pharmacists at hospital pharmacies, particularly more recent graduates, search for PI online at manufacturers' Web sites due to the ease of searching an online PDF (Expert C, 2009). Generally hospital pharmacies have computers available that are connected to the Internet (Pharmacist D, 2009), although some, such as Veterans Administration (VA) hospitals, have restricted access (Pharmacist B, 2009)

3.2.5 Clinic Pharmacists

Clinic pharmacies include drug administering or dispensing activities at surgery centers, prisons without a pharmacy, college health centers, family planning clinics, and long-term care facilities (as opposed to long-term care pharmacies, which are discussed in the next section). These might include settings in which health care providers want to administer or provide drugs to patients without requiring that patients fill their prescriptions off-site. It can also include the administration of drugs that patients cannot typically buy, such as vaccines, when administered outside of a hospital or pharmacy (Expert B, 2009). ERG was unable to locate a reliable estimate of the number of clinic pharmacists.

Depending on state regulations, clinics might contract with a pharmacist who can oversee the acquiring and dispensing of drugs. The medical director of one network of family planning clinics explained that staff members label the medications they receive for each patient, and then secure them until the contract pharmacist can review the medications and check that the medications are appropriate and labeled correctly. The medications are then made available to patients (Health Provider F, 2009).

Staff member in many clinics rarely refer to the PI, but do include Medication Guides and other patient medication information with the drugs they dispense. If the drug includes a PPI, the clinic receives as many PPIs as units of medication. In the case of oral contraceptives, a family planning clinic receives PPIs for each monthly treatment cycle. The PPIs are not inserted in the medication packaging, but accompany the bulk shipment of contraceptives. The clinic is required to provide the PPI to patients. If a patient receives contraceptives for multiple cycles, the clinic will provide one medication guide rather than one for each cycle (Health Care Provider F, 2009).

ERG assumes that virtually all clinics have at least one computer with Internet access available, and that access is unblocked.

3.2.6 Long-Term Care Pharmacists

Long-term care pharmacies service facilities that do not have a pharmacy on-site. Most of their clients are nursing homes or intermediate care facilities. They also may serve small hospitals that do not employ a full-time pharmacist. One national long-term care pharmacy company operating approximately 180 pharmacies reports that it fills prescriptions for 1.4 million people. Generally, the pharmacies are

closed to the public and pharmacists do not interact directly with patients (Pharmacist F, 2009). The HDMA (2008) estimates that there are 4,514 long-term care facilities, home health care facilities, and nursing homes, but ERG was unable to locate data on the number of pharmacists working in this setting.

Pharmacists in long-term care pharmacies rarely refer to the PI or PDR (Pharmacist F, 2009). Dispensing activities are greatly automated and often incorporate assembly lines. The drugs long-term care pharmacies dispense typically come in unit-of-use packaging, such as blister-packs, so pharmacists do not need to process the drug or to consult the paper PI on processing protocols (Pharmacist F, 2009). If questions arise regarding use of the drug, they are more likely to refer to sources of information such as American Formulary Services, Facts and Comparisons, and Clinical Pharmacology than to the PI.

While most drugs come in unit-of-use packaging, long-term care pharmacies also do drug compounding, including preparing IV therapies. Even in these cases, the pharmacist is more likely to refer to published guides specific to compounding IVs than to the PI (Pharmacist F, 2009; Pharmacist B, 2009). In some states, compounding activities conducted at long-term care pharmacies have to comply with USP 797, which establishes guidelines for "clean rooms" and prohibits computers. As with hospital pharmacies, these long-term care pharmacies would not be able to provide access in the clean room to electronic PI via the Internet (Expert B, 2009).

Internet connections are widely available in long-term care pharmacies operated by regional or national multiple-pharmacy chains (Pharmacist F, 2009).

3.2.7 Managed Care Pharmacists

Managed care pharmacies differ from other pharmacies in that pharmacists must check to determine that a prescription is approved for use under the managed care system's policies. Managed care pharmacists can be classified in three categories:

1) Administrative pharmacists who review prescriptions to determine their appropriateness for treatment

2) Pharmacists at mail order facilities who fill patient prescriptions but do not have patient contact

3) Pharmacists at managed care health systems, such as Kaiser Permanente, who fill patient prescriptions and might have patient contact (Pharmacist Association D et al., 2009).

Administrative pharmacists do not generally refer to the PI. Estimates of the number of administrative pharmacists vary widely, but one source estimates that there may be roughly 18,000 non-dispensing managed-care pharmacists (Pharmacist Association D, 2009). Their work takes place in administrative offices, and Internet access is required to review patients' prescriptions and determine their eligibility and appropriateness. Administrative pharmacists do not have the paper PI that comes affixed to medications readily available. To refer to PI, administrative pharmacists would have to access this information online, or consult other sources of information such as compendia, manufacturers' website, and Facts and Comparison (Pharmacist Association D et al., 2009).

Mail-order pharmaceutical dispensing facilities rely on automated systems to process prescriptions and distribute drugs. The pharmacist's computer software typically displays a copy of the prescription, label, and identifying information on the drug's physical appearance (Pharmacist Association D, 2009). When drugs arrive at the mail order facility, technicians typically repackage them by filling a machine or large container with the contents of the smaller bottles they have received. They

typically remove the paper PI during this step. A mail-order dispensing pharmacist might need to refer to the paper PI if there have been changes to the drug, if the regimen differs from the labeling, or if there is a black box warning. To gain access to the paper PI, the pharmacist would have to seek it out in the facility's storeroom (Pharmacist Association D et al., 2009). They typically have access to electronic information instead (Expert B, 2009).

Pharmacists who work in open pharmacies operated by managed care organizations are likely to interact with patients in a manner similar to retail pharmacists and to refer to PI in a manner similar to hospital pharmacists, given the wide range of drugs and uses that managed care pharmacists might encounter. On average, six pharmacists and 15 technicians will staff an eight-hour time-slot in a managed care pharmacy, although some states require that there be no more than two technicians per pharmacist during a shift. Pharmacists are most likely to refer to the PI if a drug is new or unfamiliar, or if they need to verify that they took into account all the information on the drug. In some cases pharmacists will take the PI for a new drug home with them (Pharmacist B, 2009). Pharmacists also provide the PI when patients request it, approximately 3 to 4 times per week. Patient requests for PI occur most often for new drugs (Pharmacist Association D et al., 2009).

If managed care pharmacists wish to reference the PI or otherwise seek out information, they can find drug information through the company's Intranet or central system. Internet access is widely available at managed care pharmacies. Both pharmacists and technicians have access to the Internet. Most mail-order pharmacists can gain access to the Internet, but not necessarily on the filling floor. Internet access may be instead available in administrative offices or where clinical decisions are being made (Pharmacist Association D et al., 2009).

3.3 CURRENT METHODS OF ACCESSING PRESCRIBING INFORMATION BY OTHER HEALTHCARE PROVIDERS

3.3.1 Healthcare Professionals in Hospitals

Healthcare professionals in hospitals rarely have access to the PI in paper form. Medications are often dispensed in unit doses. Some come in blister packs, some in vials, and others are packed by the hospital pharmacy. Some are packed into the drawers of medication dispensing carts by the pharmacy. The paper PI stays in the hospital pharmacy, so physicians and nurses on the hospital floors do not have access to them. If information on medication is needed, physicians and nurses will consult with the hospital pharmacy or the hospital's drug information center, or they will refer to sources such as the PDR, the American Hospital Formulary Service, a pocket dosage book, or information accessed via PDA (Health Care Provider A, 2009; Health Care Provider B, 2009; Pharmacist Association C, 2009). Garritty and El Emam's (2006) review of surveys of PDA use by health care providers found that PDA use was high among residents and general practitioners (with 73 and 71 percent reporting PDA use in 2004, respectively). Among those using PDAs for clinical information, 93 percent used their PDA to access drug information (Garritty and El Emam, 2006).

3.3.2 Healthcare Professionals in Clinics and Private Practice

In clinics and private practices, paper PI is used mainly when dispensing vaccines and for products with frequent label changes (Health Care Provider D, 2009; Health Care Provider C, 2009). In most other situations, nurses and physicians rely more commonly on the PDR for information (Health Care Provider C, 2009).

At one family planning clinic contacted by ERG, prescribing health care professionals rarely refer to the paper PI. They instead refer to PDR for questions regarding dosing and other drug interactions.

While all the clinics in this network have Internet access, not all family planning clinics do, and therefore not all family planning clinic prescribers are currently able to gain access to online PI (Health Care Provider F, 2009). A psychiatrist contacted by ERG reported using Epocrates (a mobile and downloaded electronic reference of drug and formulary information), both via computer and PDA, and suggested that use of Epocrates was widespread among internists. He also stated that Epocrates use was less common among psychiatrists who prescribe the same drugs routinely and are familiar with the prescribing information (Health Care Provider G, 2009). The Epocrates website asserts that one in three physicians use some version of their products (Epocrates, 2009). (Epocrates and other electronic resources are described further in section 3.4.2)

PI is included with samples, and physicians will usually pass those on to the patient (Health Care Provider D, 2009; Health Care Provider C, 2009). If no insert is available, physicians can print out the drug information available online or through third party software to provide along with a sample product. Drug representatives also provide PI along with other drug information when meeting with physicians. Physicians are most likely to read the paper PI or brochures containing the same information when encountering a new product. They might also refer to it when they have questions about drug interaction and dosage information (Health Care Provider C, 2009). With respect to physicians, frequent prescribers of a product might receive monthly visits from sales representatives who would provide updated drug information for the specific product. For most products however, sources for prescribing information include published compilations, professional communication from manufacturers, and advertising (Health Care Provider C, 2009).

3.4 FUTURE TECHNOLOGY TRENDS

The future technological developments to facilitate access to electronic PI will depend on the specific requirements of the proposed regulation. Companies who currently provide drug information to pharmacists and prescribers are in a position to take advantage of a market for such technologies, but appear to be waiting until the requirements of that market have been defined further.

Nevertheless, two field trials that PhRMA's Paperless Labeling Task Force financed point to possible technological solutions. A review of existing drug information software and dispensing software also indicates opportunities that these companies might explore to provide electronic PI through existing technologies.

3.4.1 Systems for Accessing Electronic PI

3.4.1.1 Paperless Labeling Task Force Proof-of-Concept Test

In 2002, a small proof-of-concept pilot was conducted to determine whether electronic delivery of PI is achievable in community pharmacies. During a 12-week period, two electronic PI systems from Thomson Healthcare/Health Information Designs and Etreby Computer Company (acquired in 2007 by Cerner Company) were evaluated by 5 pharmacies each in Metropolitan Washington DC. Thomson Healthcare/Health Information Designs created a small, 8x10 inch touch screen system that can sit on a pharmacy counter, with a built-in bar-code reader and a database of PI. Their system requires an electrical outlet and an analog phone line, which can be shared with a fax machine. Users of the system could quickly navigate the PI using bookmarks. The system updated itself nightly. Etreby Computer Company's system allowed pharmacists to access PI over the Internet. Users logged on to a Web site, entered a password and searched for the PI based on name, NDC number or manufacturer. It could also scan bar codes. The last ten PI changes could be reviewed and a menu was included to access the PI by section. Pharmacists thought both systems were accessible and user-friendly; however they found electronic PI difficult to read and that printing of the complete PI took too long (Ukens, 2002; Ruchalski, 2004).

3.4.1.2 Large-Scale Field Trial - Thomson Healthcare Electronic PI System

In the fall of 2004, a larger pilot was conducted at the request of PhRMA. Thomson Health Care conducted a field test of a stand-alone electronic PI system and Etreby provided an Internet solution.

Thomson's test system included an abridged database of PI for 800 drugs and had its own printer. Thus, pharmacists could print PI, if necessary. As in the proof-of-concept test, the system was an 8x10 touch screen system with a built-in bar-code reader that could sit on a pharmacy counter. It required an electrical outlet and an analog phone line, which could be shared with a fax machine. As in the proof of concept test, sections of the PI could be quickly reached with bookmarks. The system updated itself nightly.

Eighty-eight pharmacies tested the system (including 24 independent pharmacies, 61 chain pharmacies, two clinics, and one government run institution). Of these, 48 percent were able to install the solution within 15 to 30 minutes, another 48 percent required 30 to 60 minutes, and the remainder needed more than an hour (Pharmacist B, 2009). Training time was less than 15 minutes for 99 percent of participants. Five percent reported an impeded workflow and 2 percent said the system interfered with other tasks. In operations, 87 percent of participants required less than 15 seconds to access the system and all participants were always able to access the system's database. The average PI required four minutes to print 25 pages. Patients never asked for the PI, so the study administrators asked participants to print PI once in a while. Most did not need to print a PI for themselves, except for new products. The total cost to implement the system was estimated at $1,800 per site, including a printer, cables, phone jacks, and printing costs (Pharmacist B, 2009).

The average number of times pharmacies referred to electronic PI on a weekly basis doubled between the start and the end of the trial (Rupp, 2006). Seventy five pharmacists completed surveys related to their use of the system, for a response rate of 85.2 percent. Survey respondents compared the system to the paper PI on six usability characteristics. Pharmacists perceived the electronic version to be superior to the paper PI for every characteristic except space requirements for the system and its dedicated printer. While the legibility of the information was a particularly important advantage, respondents also viewed the system as superior in speed, accuracy/currency of information, ease of use, and convenience. Several respondents noted the need for faster and easier screen navigation and the ability to more easily find a specific topic on the PI, such as information on drug interactions. As this information is contained in a pull-down menu, these comments suggest the need for a more thorough orientation for future users. If all FDA-approved drugs were available in the system's database, pharmacists noted that they would be moderately more likely to use the electronic system than the paper PI. Frequent users of PI would be more likely than infrequent users to use the full-database version of the electronic system (Rupp, 2006).

3.4.1.3 Large-Scale Field Trial - Etreby

Eighty-two pharmacies tested Etreby's Internet solution (26 independent pharmacies, 54 chain pharmacies, and 2 hospitals). Installation required logging on to a Web site and adding it to a list of "favorites." For 94 percent of participants, this process required less than 15 minutes (Pharmacist B, 2009).

Workflow was not impeded for most pharmacists, except for those who used computers that shared other tasks along with Internet access. There was no delay in access. In fact, one pharmacy continued to have access during a hurricane event in Puerto Rico. Seventy two percent could access the Web site in 15 seconds or less. The average PI printed out was 19 pages in length and took one minute

and 15 seconds to print. The cost of the system per pharmacy was estimated at $500, which included printer, cables, barcode scanners and initial printing costs (Pharmacist B, 2009).

3.4.2 Software Packages

Several companies provide drug information directed at pharmacists and prescribers in paper and electronic form. These sources reformat prescribing information for ease of use and efficiency, as well as adding information provided by manufacturers, third party vendors, or the results of published studies (Drug Guide Publisher A, 2009). As discussed in Section 2, both pharmacists and prescribers are likely to refer to these sources for drug information before seeking information directly from the PI. Some of these companies also provide dispensing software, either as part of the drug database or as a separate service.

A list of drug information and dispensing software packages and their typical users is provided in Table 3-1. Drug information sources include Alchemy (Gold Standard, 2009), the American Society of Health-Systems Pharmacists' American Hospital Formulary Service, Clinical Pharmacology , Epocrates , Facts and Comparisons , Lexi-Comp , Micromedex , First DataBank's National Drug Data File, PDR.net (Thomson Reuters, 2009), and Up to Date . These typically provide much of the same information that would be found in the PI, such as dosage and administration, adverse reactions, cautions, black box warnings, chemistry, storage, and information on how the drug is supplied. Some also include other information, such as clinical information (e.g., diagnosis and disease management), brand/generic status, status as a controlled substance, license type, information for patients, syntheses of recent literature, and other services. Some of these same databases also have information on billing and pricing, and software packages like First Data Bank's Formulalist and PDX focus more exclusively on pricing and dispensing functions. These databases vary in the number of drugs they cover; for example Epocrates' Epocrates Essentials Deluxe database contains 3,300 drugs and ASHP's American Hospital Formulary Service contains 40,000. Since the 200 top-selling drugs account for more than 80 percent of all prescriptions dispensed (Verispan, 2008), these databases' lack of complete coverage would typically not be a problem. While many databases are targeted at all types of healthcare practitioners, some (such as Epocrates) are used more by physicians, while others (such as Facts and Comparisons and PDX) are used more by pharmacists.

If paper version of the PI were no longer provided, software companies could conceivably offer links to electronic PI as an additional service. Because it would be more efficient than searching a database, pharmacists also expressed an interest in being able to link directly to the full PI for each drug when selecting that drug in the dispensing system (Expert C, 2009, et al.), and this is another value-added service that might arise in the absence of the paper PI.

3.4.3 Two-Dimensional Barcoding Technology

Pharmacists expressed interest in being able to search a centralized electronic PI database by scanning the two-dimensional (2-D) barcode on drug containers. This scenario would require that all drugs' PI be available through a centralized Web site or a regularly-updated database provided through a drug information software provider. It would also require that a barcode scanner be attached to the computer used to search for drug information, and that software to read the barcode scanner be installed in the computer.

Barcodes are used with increasing frequency to provide health care more efficiently. Therefore, it is possible that companies that provide drug information will see an opportunity to add value by providing the option of purchasing and installing barcode scanners linked to their PI database. In the large-scale field trial of Thomson devices, pharmacists had the option of using a bar-code scanner, and pharmacists surveyed rated it positively (Pharmacist B, 2009).

Table 3-1. Drug Information & Dispensing Software

Software Package/ Formats	Organization	Contents	Users
Alchemy/ Desktop software with Internet updates	Gold Standard	10- and 11-digit NDCs, other package identifiers (UPC, NHRIS), product brand and generic name, active ingredients, dosage form, route of administration, strength, inactive ingredients (for allergy checking), marketer name, manufacturer name (if different from marketer), contact company (if different from marketer/ manufacturer), Orange Book/therapeutic equivalence codes, DESI indicator, brand/generic status, legend status, storage information, product attributes (sugar- free, dye-free, etc.), physical descriptors (e.g., color, shape, imprint, flavor), Drug item and package version and description, current and historical prices, price type, beginning and end dates, off market date, NCPDP billing unit, NCPDP script dosage forms, license type (e.g., NDA, ANDA, AG), replaced by product or package ID, package data (inner and outer packaging)	Retail pharmacies, hospitals, medical and pharmacy schools [a]
American Hospital Formulary Service (AHFS)/Internet, PDA	American Society of Health-System Pharmacists (ASHP)	Drug interactions, adverse reactions, cautions and toxicity, therapeutic perspective, specific dosage and administration information, preparations, chemistry, and stability, pharmacology and pharmacokinetics, contraindications, formulary management	XML files are licensed to vendors, including StatRef, Lexi-Comp, MedicinesComplete, Ovid, and First DataBank. Used by retail and hospital pharmacies, nursing stations, doctors' offices, government institutions, and third-party payers. [b]

Table 3-1. Drug Information & Dispensing Software

Software Package/ Formats	Organization	Contents	Users
Clinical Pharmacology/Internet, PDA	Gold Standard	Drugs' current and previous appearance, Medication Guides, drug interaction information, adverse event information, patient drug information, pediatric ranges, pharmaceutical manufacturer/distributor contact information, links to drug class overview, NDC number, Orange Book therapeutic equivalence ratings, legend (OTC/Rx), FDA pregnancy risk ratings by trimester, federal controlled substance schedule (where applicable), storage information, formulation and dosage form, route of administration, complete physical description, package description, therapeutic classifications, manufacturer/distributor information, IV compatibility	Retail pharmacies, hospitals, medical and pharmacy schools [a]
Epocrates Rx/PDA	Epocrates, Inc.	Adult and pediatric dosing for FDA-approved and off-label indications, black box warnings, contraindications, and cautions, serious and common adverse reactions, and drug interactions organized by clinical category, pill pictures within the drug monograph, safety and monitoring information, such as pregnancy risk categories, lactation safety ratings, monitoring parameters and therapeutic drug levels, manufacturing information including DEA/FDA status, pharmacology information including metabolism, excretion, drug class, and mechanism of action	625,000 healthcare professionals; over 225,000 are physicians, approximately 34,000 pharmacists and 20,800 pharmacy students [c]
Facts & Comparisons/Hard copy, Internet, PDA	Wolters Kluwer Health	Drug facts and comparisons, drug interaction facts, drug interaction facts: herbal supplements and food, patient information in English and Spanish, the review of natural products, nonprescription drug therapy, off-label drug facts, drug identifier, clinical calculators, black box warnings, pregnancy and lactation warnings, bioequivalency codes, investigational drugs, manufacturer index, orphan drugs, Medication Guides, FDA MedWatch links, patient assistance programs	Primarily retail and hospital pharmacists; some doctors [d]

Table 3-1. Drug Information & Dispensing Software

Software Package/ Formats	Organization	Contents	Users
Formulalist, Price Point Rx/Desktop software	First DataBank	Formulary management, current and historical pricing information, average wholesale prices	Originally pharmacies, but now equal mix of retail pharmacies, physicians, and other healthcare professionals [e]
Lexi-Comp/Hard copy, Internet, PDA	Lexi-Comp, Inc.	Drug and drug interaction information, drug allergy, drug therapy duplication, drug dose checking, information on diagnosis and disease management, formulary services, patient education resources, black box warnings,	Pharmacists, physicians, nurses, and dentists [e]
Micromedex/Internet, PDA, integration with other pharmacy software	Thomson Reuters	Comprehensive drug details, summarized drug information, facts on FDA-approved drugs, international drugs, human reproductive risks of drugs, drug interactions, identification of loose tablets & capsules, dosing information and nutrition solutions for infants, dosing calculators, information on herbals, supplements, & alternative therapies and blend conventional/alternative medicines, IV compatibility, drug usage/precautions, drug information for patients, identification of high-risk patients, Medication reconciliation, packaging information, pricing comparisons, formulary information	
National Drug Data File Plus	First DataBank	Dosage range check, drug allergy information, drug images, drug imprints, drug-alternative therapy interactions, drug-disease contraindications, drug-drug interaction, drug-food interaction, drug-lab interference, indications, IV information, Medicaid/Medicare modules, neonatal and infant dosage range check, patient education, side effects, precautions, warning labels	Originally pharmacies, but now equal mix of retail pharmacies, physicians, and other healthcare professionals [e]

Table 3-1. Drug Information & Dispensing Software

Software Package/ Formats	Organization	Contents	Users
PDX Pharmacy System/Desktop software	PDX, Inc. and National Health Information Network, Inc.	Refill/quantity tracking, generic or therapeutic substitution, OBRA drug review compliance, patient education and documentation, complete patient and family profiles, quick price quotes, discount levels, perpetual inventory with electronic ordering, multiple modem support, multiple wide-area network support, automated tasks, system integrity and security, true compounding capabilities, professional and cognitive services, electronic prescription interface for physicians, chain-wide drug utilization review, powerful pricing options, LAN and WAN communications, extensive reporting capabilities, thorough third party processing, approximate retail drug pricing for patients paying out-of-pocket	1,000 independent pharmacies and 60 chains totaling more than 10,000 pharmacies [f]
Physicians Desk Reference (PDR)/Internet, PDA	Thomson Reuters	Full FDA-approved product labeling, multi-drug interaction checker, daily news updates, PDR eBooks, concise drug information, specialty-focused resource centers, drug alerts and news, MEDLINE & Stedman's Medical Dictionary, patient education	
UpToDate/Desktop software, Internet, PDA	UpToDate	Drug database, drug interactions, adverse reactions, vaccines, new drugs/drug approvals	

Sources: Data compiled by ERG from web sites of relevant software companies and the following: [a] Thomas, 2009; [b] Shick, 2009; [b] Shick, 2009; [d] Koeneker, 2009; [e] Burnham, 2009; [f] Roth, 2009; [g] Loy, 2009.

3.4.4 Future Demand

The extent to which markets for the above technologies will become available depends on the demand for more efficient access to electronic PI. This, in turn, depends on the frequency with which pharmacists, prescribers and other PI users refer to this information. As we discussed in Section 2, the frequency with which pharmacists refer to PI ranges widely. Those pharmacists who refer to it most often might be in a position to easily search for the PI online. Chain store pharmacies that choose to block access to the Internet might be more likely to demand technologies that provide electronic PI through a regularly updated software package or device. The prescribers ERG spoke to are typically already accustomed to finding the information contained in PI through third party applications, but if PI was readily available online for free from FDA, access to such a database might be appealing if third party applications do not provide sufficient value added. Technological options to facilitate the use of electronic PI is likely to be developed once regulatory changes have been made, given the viability of the technologies tested in the small and large-scale field trials.

SECTION FOUR

METHODOLOGY IN CALCULATING COST SAVINGS AND COSTS

4.1 OVERVIEW OF THE METHODOLOGY

In profiling affected entities and estimating both cost savings and costs, ERG contacted pharmacists employed in chain drugstores, supermarkets, mass merchandisers, independent pharmacies, hospitals, clinics, mail-order facilities, and serving home health care and long term care facilities; representatives of numerous trade organizations; brand and generic pharmaceutical manufacturers; repackagers and distributors; physicians; dentists; nurses; pharmaceutical printers; and providers of data conversion services. In addition, ERG used consultants with expertise in the pharmaceutical manufacturing, repackaging, and printing industries, and where appropriate used Internet and other data sources.

4.2 ASSUMPTIONS

In order to estimate costs and based on the draft version of the regulation, ERG made the following assumptions:

1) Professional PI for all prescription drug products and biologics will no longer come in paper form, and will only be available electronically. Medication Guides, PPIs, and other patient information will continue to be distributed as they are now and will be unaffected by the regulation.

2) Manufacturers and repackagers will be required by FDA to:

   a) Include a statement with a URL on the immediate container label and, if applicable, outer container label (carton).

   b) Maintain a Toll Free phone number for requests of printed PI.

3) The costs to submit labeling electronically will be estimated as part of the final Electronic Drug Registration and Listing Systems rule (eDRLS), except for unapproved and repackaged drugs, which are not affected by that rule if they do not make labeling changes.

4) Pharmacy technicians do not dispense medication and rarely use the PI and thus the elimination of the paper version does not affect their work.

5) For infrequent users of PI, such as physicians, any costs due to time delays as estimated below for pharmacies are negligible given their sporadic use of PI.

6) Manufacturers will continue to operate the verification equipment in their packaging lines that ensures that PI is attached to the right product, because they also use this equipment for QA procedures for other labeling.

4.3 WAGE RATES

As noted in Table 4-1, ERG used Bureau of Labor Statistics (BLS) data, Medical Group Management Association (MGMA) data, and consultation with industry experts for labor costs where these are required in estimating costs associated with the regulatory change. In instances when a task

might be shared between a director of pharmacy and a staff pharmacist, ERG used an average of the two wages to approximate costs. The hourly wage estimates are also increased by the estimated average fringe benefit payment of 41 percent, as derived from BLS surveys. Based on its conversations with industry experts, ERG judges that staff members at small and medium pharmaceutical manufacturers and repackagers earn roughly the same wages (Expert A, 2009).

4.4 UNCERTAINTY ANALYSIS

A number of estimates in the cost savings and cost estimates that follow are approximations, are based on subjective judgments of persons interviewed, or are forecasts of the effects of the regulatory impacts that have not yet occurred. Thus the calculations represent considerable uncertainty. This section examines how the uncertainty of these estimates combines to represent the range of possible outcomes.

There is considerable uncertainty about some of the estimates used in extrapolating the unit cost estimates to aggregate totals. Specifically, we estimated ranges for several variables, including the number of SKUs per product affected, the number of products affected, and the number of PIs now being printed. For some estimates, such as the average number of stock keeping units (SKUs) per product affected, the range represents 100 percent or more of the estimated value.

Other estimates include some uncertainty because they represent difficult-to-observe aspects of normal operations. For example, no data sources have rigorously generated data on the extent and current frequency of PI use or on the cost of substituting other information for PIs. Such estimates are based on interview surveys among participants (such as pharmacists) who can only estimate the frequency of their actions during the workday.

Other inputs to the cost model are presented as point estimates because there is a recognized source for the information provided, or the range of likely values is not sufficiently wide as to be crucial to the analysis. For example, we were able to obtain reliable data on the number of pharmacies, and on the average employment among pharmacies. We also have useful average data on wage rates among pharmacy employees and other inputs to the analysis.

As noted below, the estimated ranges for many of the inputs produce a range for the final cost and cost savings estimates. These ranges reflect the uncertainties of the inputs and their combined impact is to produce a wide range for the final cost and cost savings totals.

Table 4-1. Wage Rates Used in Cost Estimates

Job Category [a]	Hourly Wage	Fringe Benefits [b]	Loaded Wage	Source
Director of pharmacy/Senior pharmacist	$50.13	$20.55	$70.68	BLS, 2007a
Staff pharmacist	$47.58	$19.51	$67.09	BLS, 2007a
Pharmacy technician	$13.25	$5.43	$18.68	BLS, 2007a
Physician	$91.61	$37.56	$129.17	MGMA, 2008
Network & systems administrator	$37.69	$15.45	$53.14	BLS, 2007c
IT Manager	$58.25	$23.88	$82.13	BLS, 2008c
Manufacturing managers				
Small/Medium or Repackager	$50.05	$20.52	$70.57	BLS, 2008c
Large	$71.50	$29.32	$100.82	BLS, 2008c
Generic	$57.20	$23.45	$80.65	BLS, 2008c
Manufacturing production workers				
Small/Medium or Repackager	$14.89	$6.11	$21.00	BLS, 2007d; Expert A, 2009
Large	$19.15	$7.85	$27.00	BLS, 2007d; Expert A, 2009
Generic	$17.73	$7.27	$25.00	BLS, 2007d; Expert A, 2009
Regulatory affairs officer				
Small/Medium or Repackager	$24.82	$10.18	$35.00	BLS, 2007d; Expert A, 2009
Large	$35.46	$14.54	$50.00	BLS, 2007d; Expert A, 2009
Generic	$28.37	$11.63	$40.00	BLS, 2007d; Expert A, 2009
Switchboard operator				
Small/Medium or Repackager	$10.64	$4.36	$15.00	BLS, 2007e; Expert A, 2009
Large	$12.77	$5.23	$18.00	BLS, 2007e; Expert A, 2009
Generic	$11.35	$4.65	$16.00	BLS, 2007e; Expert A, 2009
Manager	$54.26	$22.25	$76.51	BLS, 2008b

[a] Mean hourly wage estimates

[b] Based on a 41% fringe benefits rate for private industry (BLS, 2008a).

SECTION FIVE

COST SAVINGS OF THE PROPOSED RULE

Manufacturers and repackagers of prescription drugs and biologics will realize significant savings if the proposed rule is implemented because they no longer have to print PI. The volume of inserts that are produced per year is substantial and thus the rule provides significant cost savings to manufacturers and repackagers.

5.1 UNIT AND TOTAL COST SAVINGS

5.1.1 Cost Savings for Manufacturers

Manufacturers (or in many cases the contract packagers with whom they do business) will realize cost savings by switching from paper to electronic PIs. One source of savings comes from eliminating the costs of storing and printing inserts. Manufacturers typically keep a few months worth of paper PI inventory stored in a warehouse. The amount stored is dependent on how frequently and how much of the product is produced. To estimate costs for this component, ERG used an industrial rent cost of $4.90 per square foot per year (Milliken Institute, 2007) and assumed that the PI of approximately four SKUs might take up approximately one square foot of warehouse space, suggesting a per-SKU storage cost of $1.23. An industry expert, however, suggested that these costs may be slightly higher, and vary by establishment size (Expert A, 2009). Accordingly, ERG estimates annual storage costs for paper inserts per SKU of $1.40 for small and medium manufacturers and $1.50 for large and generic manufacturers.

There is also a cost savings associated with no longer incurring inventory loss of paper, as label changes will no longer mean having to discard any paper PI that was printed before the change. These changes may be particularly frequent for new products (Data Conversion Service Provider A, 2009) or products like anti-depressants and sleep medications (Manufacturer A, 2009). ERG received one estimate that these savings may amount to $346,000 annually for a manufacturer of products with more frequent PI changes (Manufacturer A, 2009). These savings will vary widely, however, across manufacturers because they depend on the assortment of products manufactured. Given this variability and the subsequent difficulty of accurately estimating these savings, we do not include this figure in our analysis.

In order to estimate the number of SKUs affected, ERG uses FDA's estimate that manufacturers produce 50,000 SKUs and repackagers 120,000 to 150,000 SKUs, ERG calculated the midpoint of the estimates of the number of SKUs produced by repackagers (135,000), and totaled the number of SKUs produced overall (185,000). This suggests that manufacturers produce 27 percent of SKUs, while repackagers produce 73 percent. Based on the HMDA's (2008) data for brand name and generic pharmaceuticals, ERG further assumes that small manufacturers produce 25 percent of SKUs, large manufacturers 25 percent, and generic manufacturers 50 percent.

In order to estimate the units of PI produced annually, ERG began with FDA's (2006) estimate that there are 2.6 billion pieces of trade labeling accompanying prescription drug products annually, including prescriptions dispensed in both retail settings and hospitals. Because FDA's data does not distinguish between PI produced by manufacturers and repackagers, we extrapolate from our SKU calculations and assume that manufacturers produce 27 percent of PI (or 702 million units). Next, ERG distributed the cost savings production of PI among small/medium, large and generic pharmaceutical manufacturers. Based on IMS Health data published in the 2008-2009 HDMA Factbook (HDMA, 2008) on the distribution of prescriptions between brand and generic manufacturers, ERG allocated production

of PI as follows: small/medium manufacturers produce 10 percent, large manufacturers produce 40 percent of all PI, and generic manufacturers produce 50 percent[4]. In order to perform an uncertainty analysis, we subtract and add 15 percent to generate high and low estimates of the number of units of PI produced annually for each category of manufacturer.

Finally, we estimate that printing and folding paper PIs costs from $0.04 to $0.07 per insert (Printer A, 2009), and that inserting/attaching paper PIs and performing quality assurance checks costs $0.005 per insert (Expert A, 2009).

With these assumptions total annual cost savings for cessation of paper PI are between $2.7 and $6.1 million for small and medium manufacturers, between $8.1 and $20.7 million for large manufacturers, and between $10.2 and $25.9 million for generic manufacturers (see Table 5-1). Summing these costs across all manufacturers results in total cost savings of between $21 million and $52.6 million.

5.1.2 Cost Savings for Repackagers

Like manufacturers, repackagers, which for this analysis includes relabelers and the manufacturers of products distributed via private label, will realize significant cost savings by switching from electronic to paper PI. Repackagers also currently store a few months of paper PI inventory which will no longer be required under the proposed rule.

As detailed above in section 5.1.1, we use data supplied by FDA to estimate that repackagers produce 120,000 to 150,000 SKUs. We then use the manufacturer/repackager SKU distribution to estimate that repackagers generate 73 percent of all PI units produced by the industry. In order to generate the uncertainty analysis for units of PI, we subtract and add 15 percent to the total units of PI, suggesting that repackagers produce between 1.6 billion and 2.2 billion units of PI annually.

As in the case of manufacturers, ERG estimated the current cost of paper PI storage by using an industrial rent cost of $4.90 per square foot per year (Milliken Institute, 2007) and assuming that the PI of approximately four SKUs might take up approximately 1 square foot of warehouse space, suggesting a per-SKU storage cost of $1.23, which we adjusted to $1.40 per-SKU on the advice of an industry expert (Expert A, 2009). Multiplying this number by the number of SKUs produces an estimated cost savings of between $22,500 and $37,500.

Repackagers incur similar printing and folding costs to manufacturers, which are estimated at $0.04 to $0.07 per insert (Printer A, 2009). Inserting/attaching paper PIs and performing quality assurance checks costs are also the same at $0.005 per insert (Expert A, 2009). Multiplying these costs by the number of PI suggests that repackagers will save between $72.6 million and $163.7 million annually as a result of no longer having to print paper PI.

Totaling the costs for storage, printing, and folding of PI suggests annual cost savings for repackagers of between $72.8 and $163.9 million (see Table 5-2).

[4] Note that the estimated distribution of SKUs does not match the estimated distribution of PI production, as larger companies produce more high-volume “blockbuster” drugs that require a high ratio of copies of paper PI to SKUs.

Table 5-1. Manufacturers – Unit and Total Cost Savings

	Small/Medium Brand Manufacturers		Large Brand Manufacturers		Generic Manufacturers		Source
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate	
Storage and Printing Cost Savings							
Annual storage cost for inserts per SKU	$1.40	$1.40	$1.50	$1.50	$1.50	$1.50	Expert A, 2009; ERG estimate
Prescription SKUs affected	7,500	12,500	7,500	12,500	15,000	25,000	ERG, 2008; HDMA, 2008; FDA estimate
Total annual storage cost savings	$10,500	$17,500	$11,250	$18,750	$22,500	$37,500	
Printing and folding per insert	$0.04	$0.07	$0.03	$0.06	$0.03	$0.06	Printer A, 2009
Quality assurance and inserting/attaching paper insert per insert	$0.005	$0.005	$0.004	$0.004	$0.004	$0.004	Expert A, 2009; ERG estimate
Total units PI produced annually	59,670,000	80,730,000	238,680,000	322,920,000	298,350,000	403,650,000	ERG estimate
Total annual PI printing/folding cost savings	$2,685,150	$6,054,750	$8,115,120	$20,666,880	$10,143,900	$25,833,600	
Total annual cost savings	**$2,695,650**	**$6,072,250**	**$8,126,370**	**$20,685,630**	**$10,166,400**	**$25,871,100**	

Table 5-2. Repackagers – Unit and Total Cost Savings

	Low Estimate	High Estimate	Source
Storage and Printing Cost Savings			
Annual storage cost for inserts per SKU	$1.40	$1.40	Expert A, 2009; ERG estimate
Prescription SKUs affected	120,000	150,000	FDA estimate
Total annual storage cost savings	$168,000	$210,000	
Printing and folding per insert	$0.04	$0.07	Printer A, 2009
Quality assurance and inserting/attaching paper insert per insert	$0.005	$0.005	Expert A, 2009; ERG estimate
Total units PI produced annually	1,613,300,000	2,182,700,000	ERG estimate
Total annual PI printing/folding cost savings	$72,598,500	$163,702,500	
Total annual cost savings	**$72,766,500**	**$163,912,500**	

5.1.3 Total Cost Savings for Manufacturer and Repackagers

Annual cost savings total between $21 million and $52.6 million for manufacturers and between $72.8 million and $163.9 million for repackagers, for industry-wide cost savings of between $93.8 million and $216.5 million (see Table 5-3).

Table 5-3. Annual Cost Savings Summary

	Low Estimate	High Estimate
Manufacturers	$20,988,420	$52,628,980
Repackagers	$72,766,500	$163,912,500
Total Cost Savings	**$93,754,920**	**$216,541,480**

5.2 ANNUALIZED COST SAVINGS FOR MANUFACTURERS AND REPACKAGERS

Compliance with the proposed rule will generate a net savings for manufacturers and repackagers, but in the case of the cost savings described above all costs will be incurred on an annual basis and no annualization is required.

SECTION SIX

COSTS OF THE PROPOSED RULE

This section discusses the costs associated with the proposed paperless labeling rule as they will affect pharmacies, other users of PI, manufacturers, repackagers, and printers. While FDA does not regulate pharmacies, the proposed rule will impact them to the extent that they use the paper PI to obtain drug information. Other users of the paper PI, such as physicians and clinics, will be similarly affected. Manufacturers and repackagers will incur some costs to add a few lines of text to labeling on containers and cartons (if applicable) to refer to the Internet address (i.e., the URL) where the PI can be found. They will also be required to provide a toll free telephone number for PI. Due to the specialized nature of the production of prescription drug PI, printers that produce the PI and their paper suppliers will see a significant drop in business.

6.1 UNIT AND TOTAL COMPLIANCE COSTS

6.1.1 Pharmacies

Costs will accrue to many pharmacies in order to access electronic PI. The cost savings realized by manufacturers will in part be transferred to pharmacies, as the printing formerly done by manufacturers will now be done by pharmacies when they deem it necessary. Further, in order to print electronic PI, some pharmacies will need to invest in the infrastructure to do so, including Internet access and computer hardware. Pharmacists will also spend additional time on training and more time searching for and printing PI than they currently do.

6.1.2 Chain Pharmacies

The NACDS (2007) reports that there are 38,695 chain pharmacies. Most of these pharmacies make use of paper PI to varying degrees. Some report relying exclusively on electronic resources (Pharmacist G, 2009), whereas others report referring to either the electronic or paper version of the PI for 10 percent of prescriptions filled (Pharmacist B, 2009), or at least once a day (Pharmacist A et al, 2009; Expert C, 2009). Within or across pharmacies, the extent of reliance on paper versus electronic PI often depends on the age of the pharmacist. Younger pharmacists have greater comfort using electronic resources to obtain drug information (Expert C, 2009).

Internet Access

In their comments to FDA on the Electronic Distribution of Prescription Information (2007), the American Pharmacists Association (APhA) indicated that only 65 percent of their surveyed members had the technological capacity to gain access to electronic PI, while 23 percent did not have access to the Internet or the technology needed to accommodate a switchover to electronic PI. Ten percent of those surveyed at the time were in the process of improving their pharmacies' technological capabilities, so the percentage of pharmacists not equipped to access electronic PI has likely decreased since the survey was taken. Pharmacist Association B (2009) estimates that 99 percent of independent pharmacies have access to the Internet, and ERG assumes that a similar proportion of chain pharmacies currently have Internet access and thus does not include any costs for pharmacies to gain Internet access.

Some chains, such as Rite Aid, block their pharmacy staff from Internet access (NACDS, 2009). To access a Web Portal with PI data, therefore, these chains would have to unblock access to that domain. Website access is managed at the headquarters level and the HMDA (2008) estimates that there are 244 chain store headquarters. A network systems administrator at the company's headquarters would need to

provide each store with open access to the centralized FDA Web Portal. Pharmacist Association A (2009) estimated that roughly 10,000 establishments, (which translates to 26 percent of chain store establishments with pharmacies) currently block Internet access. Based on conversations with network systems administration staff, ERG determined that a network systems administrator typically requires between three and eight hours to provide and maintain access to a website or websites containing electronic PI. At a rate of $53.14 per hour for a network and systems administrator, each chain will incur cots of between $159 and $425 per year to provide Internet access to PIs on the Internet. Across all chains, this would require an investment of between $10,043 and $26,781 per year (see Table 6-1).

Table 6-1. Chain Pharmacies – Internet Access Costs

Cost	Low Estimate	High Estimate	Source
Internet Access			
Annual hours by network systems administrator to maintain access to FDA website	3	8	ERG estimate
Network systems administrator wage	$53.14	$53.14	BLS, 2007c
Unit annual cost	$159	$425	
Percentage of pharmacies with blocked Internet access	26%	26%	NACDS, 2009
Number of chain headquarters	244	244	HDMA, 2008
Total annual cost	**$10,043**	**$26,781**	

Accessing and Printing Delays

Accessing and printing the PI from a Web Portal could result in some delays. In some instances, download speeds might be slow and the PI might take longer to access electronically than it would take to pull the PI off a container. Printers might jam or be busy or otherwise require additional time from the pharmacist to print the PI.

In order to estimate how often pharmacists refer to PI and thus how often accessing and printing delays might affect them, ERG referred to a study conducted by Thomson Healthcare. In 2004, 75 pharmacists were asked to report how often they refer to the paper PI for drug information. Almost half of respondents (49.3 percent) responded once or twice a month, almost one third reported that they refer to the PI once or twice a week, nine respondents (12 percent) indicated that they refer to the paper PI at least daily, and seven (9.3 percent) rarely refer to it (Rupp, 2006). ERG calculated a weighted average of these responses and estimated that the PI is consulted roughly 88 times per year by each pharmacist, whether due to patient requests for the information or for the pharmacists own needs (Rupp, 2006).

We then assumed that pharmacists would print the PI between a third and two thirds of the time they referred to it (Expert C, 2009; Pharmacist B, 2009; Pharmacist Association A, 2009), or between 29 and 58 times per year per pharmacist. Pharmacist B (2009) estimates that 10 percent of the instances that PI is consulted and printed result in delays that require additional time from the pharmacist. ERG estimates roughly an average of 10 minutes for each instance of additional time required from the pharmacist, based on common time delays due to Internet speed or printing problems. Assuming an average of three pharmacists per pharmacy and weighting wages to reflect a variation in seniority of staff members who might need to access the PI, delays in accessing and printing electronic PI would cost between $397 and $496 per pharmacy and between $15.4 million and $19.2 million for all chain pharmacies (see Table 6-2).

Table 6-2. Chain Pharmacies – Accessing and Printing Delays

Cost	Low Estimate	High Estimate	Source
Delays			
Frequency that PI is consulted annually per pharmacist	88	88	Rupp, 2006
Expected frequency of printing PI as a percentage of consulting frequency	33%	67%	Pharmacist Association C, 2009
Expected frequency of printing electronic PI annually per pharmacist	29	58	
Annual number of copies of PI with delays (searching, printing)	12	15	Pharmacist B, 2009
Length of delay in minutes for searching/printing	10	10	ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Unit cost per pharmacist	$132	$165	
Number of pharmacists per pharmacy	3	3	Pharmacist A et al., 2009
Unit annual cost	$397	$496	
Number of chain pharmacies	38,695	38,695	NACDS, 2007
Total annual cost	**$15,350,920**	**$19,188,650**	

Printing Costs

ERG estimates that PI will need to be printed by pharmacists at chain pharmacies between 29 and 58 times per year per pharmacist (Expert C, 2009; Pharmacist B, 2009; Pharmacist Association A, 2009). At a cost of 4 cents per page and a length of between 20 and 30 pages per copy of the PI, it will cost from $0.80 to $1.20 to print one copy of the PI in the pharmacy (PCSupportTips.com, 2008; TopTenReviews.com, 2009; Manufacturer D, 2009; Pharmacist B, 2009). Pharmacist B (2009) reported in the Thomson Healthcare and Etreby studies that PI required anywhere from one minute and 15 seconds to four minutes to print. However, ERG assumes that pharmacists will be able to carry out other tasks while the PI is printing, and so estimates a minimal 30 seconds to one minute for printing. This translates into a labor cost of between $0.57 and $1.13 per copy of the PI to account for time by a director of pharmacy or staff pharmacist to print the PI. Assuming three pharmacists per pharmacy (Pharmacist A, 2009; HDMA, 2008), printing costs are between $120 and $408 per year per pharmacy. Total costs for all 38,695 chain pharmacies are estimated to reach between $4.6 and $15.8 million per year (see Table 6-3).

Table 6-3. Chain Pharmacies – Printing Costs

Cost	Low Estimate	High Estimate	Source
Printing			
Expected frequency of printing electronic PI annually per pharmacist	29	58	
Cost per page (including ink and paper)	$0.04	$0.04	PCSupportTips.com, 2008; TopTenReviews.com, 2009
Average number of pages per copy of PI	20	30	Manufacturer D, 2009; Pharmacist B, 2009; FDA estimate
Average material cost to print one copy of PI	$0.80	$1.20	
Minutes required to print average PI	0.5	1	Pharmacist B, 2009; ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Average labor cost to print one copy of PI	$0.57	$1.13	
Unit cost per pharmacist	$40	$136	
Number of pharmacists per pharmacy	3	3	Pharmacist A et al., 2009
Unit annual cost	$120	$408	
Number of chain pharmacies	38,695	38,695	NACDS, 2007
Total annual cost	**$4,628,382**	**$15,804,010**	

Computer Hardware

Pharmacists we interviewed stated that nearly all pharmacies use printers to print drug labels and consumer medication information. Some indicated that these printers could not be easily used to print PI because all available trays contain specialized labeling paper, while others stated that an option to print on standard 8 ½ x 11-inch paper already exists in many pharmacies. Without a reliable estimate of printer availability, we have assumed that the 33 percent of pharmacies would need to purchase a printer for the purpose of printing PI. A basic laser printer costs between $100 and $400 and operating and maintenance costs generally run about 10 percent of capital costs.

All the pharmacists we contacted asserted that pharmacies nearly always have a computer that is reserved for non-dispensing activities. However some small percentage of these members might also need to purchase a computer. We assume that this percentage is the same as the number of pharmacies without Internet access, 1 percent. Desktop computers cost between $400 and $700 and operating and maintenance costs generally run about 10 percent of capital costs. Totaling these costs across all 38,695 chain pharmacies results in one-time costs of between $1.4 and $5.4 million, and annual operating and maintenance costs of between $0.1 million and $0.5 million.

Table 6-4. Chain Pharmacies – Computer Hardware Costs

Cost	Low Estimate	High Estimate	Source
Computer Hardware			
Cost of dedicated laser printer	$100	$400	Costhelper.com, 2009; PCSupportTips.com, 2008
Cost of dedicated computer	$400	$700	Frucci, 2008
Unit one-time cost	$500	$1,100	
Printer operating and maintenance costs	$10	$40	ERG estimate
Computer operating and maintenance costs	$40	$70	ERG estimate
Annual Operating and Maintenance Costs	$50	$110	
Percentage of pharmacies that need printers	33%	33%	APhA, 2007
Percentage of pharmacies that need computers	1%	1%	Pharmacist Association E, 2009
Number of chain pharmacies	38,695	38,695	NACDS, 2007
Total one-time cost	$1,431,715	$5,378,605	
Total annual cost	**$143,172**	**$537,861**	

Training

ERG assumes that training requirements will be minimal. When field trials were conducted of the Etreby solution, 90 percent of participating pharmacists familiarized themselves with the system in less than an hour (Pharmacist B, 2009). Most pharmacists are very comfortable with the Internet and will have no problem understanding how to search for the data. ERG judges that the majority will take between 15 and 30 minutes to become comfortable with searching a website for PI. ERG estimates a unit cost for training of $51 to $102 per pharmacy, assuming between 15 and 30 minutes of training for an average of three pharmacists per pharmacy (Pharmacist A et al., 2009). Given the low turn-over rates for pharmacists and relative ease with which someone can familiarize themselves with a website, ERG assumed that annual costs associated with staff turnover would be negligible. Total one-time training costs are estimated at between $2 million and $3.9 million for all 38,695 chain pharmacies (see Table 6-5).

Table 6-5. Chain Pharmacies – Training Costs

Cost	Low Estimate	High Estimate	Source
Training			
Number of hours of training per staff member	0.25	0.5	ERG estimate
Number of pharmacy staff to be trained	3	3	Pharmacist A et al., 2009
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Unit one-time cost	$51	$102	
Number of chain pharmacies	38,695	38,695	NACDS, 2007
Total one-time cost	**$1,973,058**	**$3,946,117**	

6.1.3 Independent Pharmacies

According to NACDS (2007), there are 16,921 independent pharmacies. The process of accessing PI at independent pharmacies is similar to that at chain pharmacies, except that blocking of websites is much less common. Based on conversations with industry experts, ERG assumed that a very small percentage might still need to unblock Internet access, but the cost is expected to be negligible and is not estimated here (Pharmacist Association B, 2009).

Accessing and Printing Delays

As in the case of chain pharmacies, we assume that the PI is consulted an average of 88 times per year per pharmacist (Rupp, 2006) and that pharmacists will print the PI between one third and two thirds of the time, with a ten minute delay in access or printing occurring ten percent of those times. Using a blended wage of $67.99 for directors of pharmacy and staff pharmacists and assuming an average of three pharmacists per independent pharmacy (NCPA, 2008), annual unit costs per pharmacy are estimated to be between $397 and $496. Summing across all 16,921 independent pharmacies (NACDS, 2007) results in total annual costs for accessing and printing delays of between $6.7 million and $8.4 million (see Table 6-6).

Table 6-6. Independent Pharmacies – Accessing and Printing Delays

Cost	Low Estimate	High Estimate	Source
Delays			
Frequency that PI is consulted or asked for by patients annually per pharmacist	88	88	Rupp, 2006
Expected frequency of printing PI as a percentage of consulting frequency	33%	67%	Pharmacist Association C, 2009
Expected frequency of printing electronic PI annually per pharmacist	29	58	
Annual number of copies of PI with delays (searching, printing)	12	15	Pharmacist B, 2009
Length of delay in minutes for searching/printing	10	10	ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Unit cost per pharmacist	$132	$165	
Number of pharmacists per pharmacy	3	3	NCPA, 2008
Unit annual cost	$397	$496	
Number of independent pharmacies	16,921	16,921	NACDS, 2007
Total annual cost	**$6,712,829**	**$8,391,036**	

Printing Costs

Again assuming that pharmacists will print the PI between 29 and 58 times per year per pharmacist, a cost of 4 cents per page, and a length of between 20 and 30 pages per copy of the PI, it will cost from $0.80 to $1.20 to print one copy of the PI in the pharmacy (PCSupportTips.com, 2008; TopTenReviews.com, 2009; Manufacturer D, 2009; Pharmacist B, 2009). Assuming the pharmacist devotes between 20 seconds to one minute to the task of printing, this translates into a labor cost of between $0.57 and $1.13 per copy of the PI to account for time by a director of pharmacy or staff

pharmacist to print the PI, for a unit cost per pharmacist of between $40 and $136, and a unit cost per independent pharmacy of between $120 and $408. Total annual printing costs are estimated at between $2 million and $6.9 million (see Table 6-7).

Table 6-7. Independent Pharmacies – Printing Costs

Cost	Low Estimate	High Estimate	Source
Printing			
Expected frequency of printing electronic PI annually per pharmacist	29	58	
Cost per page (including ink and paper)	$0.04	$0.04	PCSupportTips.com, 2008; TopTenReviews.com, 2009
Average number of pages per copy of PI	20	30	Manufacturer D, 2009; Pharmacist B, 2009
Average material cost to print one copy of PI	$0.80	$1.20	
Minutes required to print average PI	0.5	1	Pharmacist B, 2009; ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Average labor cost to print one copy of PI	$0.57	$1.13	
Unit cost per pharmacist	$40	$136	
Number of pharmacists per pharmacy	3	3	NCPA, 2009
Unit annual cost	$120	$408	
Number of independent pharmacies	16,921	16,921	NACDS, 2007
Total annual cost	**$2,023,953**	**$6,910,962**	

Computer Hardware

As in the case of chain pharmacies, we have assumed that the 33 percent of pharmacies would need to purchase a printer for the purpose of printing PI at a cost of between $100 and $400, with annual operating and maintenance costs of 10 percent of capital costs. We again assume that one percent of pharmacies might also need to purchase a computer at a cost of between $400 and $700, with annual operating and maintenance costs amounting to 10 percent of capital costs. This results in total one-time costs of between $0.6 million and $2.4 million for computer hardware purchases, with total annual operating and maintenance costs of between $62,608 and $235,202 (see Table 6-8).

Table 6-8. Independent Pharmacies – Computer Hardware Costs

Cost	Low Estimate	High Estimate	Source
Computer Hardware			
Cost of dedicated printer	$100	$400	Costhelper.com, 2009; PCSupportTips.com, 2008
Cost of dedicated computer	$400	$700	Frucci, 2008
Unit one-time cost	$500	$1,100	
Printer operating and maintenance costs	$10	$40	ERG estimate
Computer operating and maintenance costs	$40	$70	ERG estimate
Annual Operating and Maintenance Costs	$50	$110	

Table 6-8. Independent Pharmacies – Computer Hardware Costs

Cost	Low Estimate	High Estimate	Source
Percentage of pharmacies that need printers	33%	33%	APhA, 2007
Percentage of pharmacies that need computers	1%	1%	Pharmacist Association E, 2009
Number of independent pharmacies	16,921	16,921	NACDS, 2007
Total one-time cost	$626,077	$2,352,019	
Total annual cost	**$62,608**	**$235,202**	

Training

ERG assumes that training requirements will be minimal, requiring between 15 and 30 minutes per pharmacist. ERG estimates a unit cost for training of $51 to $102 per pharmacy, and total one-time costs for training for all independent pharmacies of between $0.9 million and $1.7 million (see Table 6-9).

Table 6-9. Independent Pharmacies – Training Costs

Cost	Low Estimate	High Estimate	Source
Training			
Number of hours of training per staff member	0.25	0.5	ERG estimate
Number of pharmacy staff to be trained	3	3	NCPA, 2008
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Unit one-time cost	$51	$102	
Number of independent pharmacies	16,921	16,921	NACDS, 2007
Total one-time cost	**$862,802**	**$1,725,604**	

6.1.4 Hospital Pharmacies

Hospital pharmacies also incur similar costs to chain and independent pharmacies. According to the HMDA, there are 10,362 hospital pharmacies (all pharmacies with a hospital address) (HDMA, 2008).

Internet Access

While hospitals have Internet infrastructure available, several discussions with hospital pharmacists (Pharmacist D, 2009; Pharmacist B, 2009) indicate that many hospitals completely or partially block Internet access. Based on discussions with industry contacts, ERG estimated that approximately 50 percent of hospitals and other institutional pharmacies have restricted Internet access. This translates into a total annual cost of between $0.8 million and $2.2 million for all hospitals to unblock Internet access (see Table 6-10).

Table 6-10. Hospital Pharmacies – Internet Access

Cost	Low Estimate	High Estimate	Source
Internet Access			

Table 6-10. Hospital Pharmacies – Internet Access

Cost	Low Estimate	High Estimate	Source
Annual hours by network systems administrator to maintain access to FDA website	3	8	ERG estimate
Network systems administrator wage	$53.14	$53.14	BLS, 2007c
Unit annual cost	$159	$425	
Percentage of pharmacies with blocked Internet access	50%	50%	ERG estimate
Number of pharmacies	10,362	10,362	HDMA, 2008
Total annual cost	**$826,000**	**$2,202,667**	

Accessing and Printing Delays

There was little consensus among pharmacists regarding the use of PI at pharmacies. Pharmacist D (2009) reported that pharmacists consult PI up to 10 times a week and several noted that the use of PI at hospitals tends to be higher than at chain and independent pharmacies (Expert B, 2009, Pharmacist B, 2009, Pharmacist D, 2009). Another pharmacist with hospital experience noted that he and others rarely or never used the PI in their hospital work. While hospital pharmacists generally have less direct patient interaction, they are likely to take unusual conditions, interactions, or dosing into account when dispensing drugs. They thus have a greater range of activity, suggesting a greater need for PI. They are also more likely to be engaged in clinical trials of new products. Taking these data points into account, ERG assumed that the average hospital pharmacist consults PI roughly 3 times a week, or 156 times per year.

While a given hospital pharmacy typically has 11 staff members (AHA, 2007), we estimate that there are an average of four pharmacists working in the pharmacy on a single day. As in the case of chain and independent pharmacies, we assume that hospital pharmacists print out the PI between one third and two thirds of the time, or between 52 and 104 times per year. We assume that 10 percent of these instances will involve delays in accessing or printing the PI, and use a blended wage of $67.99 for directors of pharmacy and staff pharmacists. This suggests unit costs per pharmacist of between $236 and $295 per year. Assuming there are an average of four pharmacists per hospital pharmacy on a given day suggests unit costs per hospital pharmacy of between $943 and $1,178, resulting in total annual costs across all 10,362 hospital pharmacies of between $9.8 million and $12.2 million (see Table 6-11).

Table 6-11. Hospital Pharmacies – Accessing and Printing Delays

Cost	Low Estimate	High Estimate	Source
Delays			
Frequency that PI is consulted annually per pharmacist	156	156	ERG estimate
Expected frequency of printing PI as a percentage of consulting frequency	33%	67%	Pharmacist Association C, 2009
Expected frequency of printing electronic PI annually per pharmacist	52	104	
Annual number of copies of PI with delays (searching, printing)	21	26	Pharmacist B, 2009
Length of delay in minutes	10	10	ERG estimate

Table 6-11. Hospital Pharmacies – Accessing and Printing Delays

Cost	Low Estimate	High Estimate	Source
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Unit cost per pharmacist	$236	$295	
Number of pharmacists per pharmacy	4	4	ERG estimate
Unit annual cost	$943	$1,178	
Number of pharmacies	10,362	10,362	HDMA, 2008
Total annual cost	**$9,768,761**	**$12,210,951**	

Printing Costs

Some hospital pharmacists like to read a paper copy of the PI for a new drug when they receive it, before receiving prescriptions for the drug. If the product is new or uncommon, they may also want to hand the printed insert to the doctor treating the patient. As in the case of chain and independent pharmacies, we assume that hospital pharmacists will print the PI between one third and two thirds of the time they refer to it, or between 52 and 104 times per year (including instances in which a pharmacist or technician needs to print out the PI before referring to it in the clean rooms). Using the same assumptions about printing costs and wages as in the case of chain and independent pharmacies suggests a unit annual cost per pharmacy of between $284 and $971. Totaling this cost over all 10,362 hospital pharmacies suggests total annual printing costs of between $2.9 million and $10.1 million (see Table 6-12).

Table 6-12. Hospital Pharmacies – Printing Costs

Cost	Low Estimate	High Estimate	Source
Printing			
Expected frequency of printing electronic PI annually per pharmacist	52	104	
Cost per page (including ink and paper)	$0.04	$0.04	PCSupportTips.com, 2008; TopTenReviews.com, 2009
Average number of pages per copy of PI	20	30	Manufacturer D, 2009; Pharmacist B, 2009
Average material cost to print one copy of PI	$0.80	$1.20	
Minutes required to print average PI	0.5	1	Pharmacist B, 2009; ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Average labor cost to print one copy of the PI	$0.57	$1.13	
Unit cost per pharmacist	$71	$243	
Number of pharmacists per pharmacy	4	4	ERG estimate
Unit annual cost	$284	$971	
Number of pharmacies	10,362	10,362	HDMA, 2008
Total annual cost	**$2,945,332**	**$10,057,091**	

Computer Hardware

The hardware investment required for printing PI is again similar to that of chain and independent pharmacies. ERG assumed that some hospital pharmacies might also need to purchase additional equipment because their current hardware is already used extensively. We assumed that 33 percent would need to purchase an additional printers and 1 percent would need computers. Hospitals are expected to incur a one-time total cost of between $0.4 million and $1.4 million to purchase hardware and an annual cost of between $38,339 and $0.1 million for operating and maintenance costs.

Table 6-13. Hospital Pharmacies – Computer Hardware Costs

Cost	Low Estimate	High Estimate	Source
Computer Hardware			
Cost of dedicated printer	$100	$400	Costhelper.com, 2009; PCSupportTips.com, 2008
Cost of dedicated computer	$400	$700	Frucci, 2008
Unit one-time cost	$500	$1,100	
Printer operating and maintenance costs	$10	$40	ERG estimate
Computer operating and maintenance costs	$40	$70	ERG estimate
Annual Operating and Maintenance Costs	$50	$110	
Percentage of pharmacies that need printers	33%	33%	APhA, 2007
Percentage of pharmacies that need computers	1%	1%	Pharmacist Association E, 2009
Number of independent pharmacies	10,362	10,362	HDMA, 2008
Total one-time cost	$383,394	$1,440,318	
Total annual cost	**$38,339**	**$144,032**	

Training

Using the same assumptions about training as in the case of chain and independent pharmacies but assuming an average of 11 pharmacists per pharmacy (AHA, 2007), we estimate one-time training costs of between $187 and $374 per pharmacy and between $1.9 million and $3.9 million for all 10,362 hospital pharmacies (see Table 6-14).

Table 6-14. Hospital Pharmacies – Training Costs

Cost	Low Estimate	High Estimate	Source
Training			
Number of hours of training per staff member	0.25	0.5	ERG estimate
Number of pharmacy staff to be trained	11	11	AHA, 2007
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	ERG estimate
Unit one-time cost	$187	$374	
Number of pharmacies	10,362	10,362	HDMA, 2008
Total one-time cost	**$1,937,314**	**$3,874,629**	

6.1.5 Infrequent Users of PI

Infrequent users of PI include physicians and the staff at clinics, infusion centers, and pharmacies servicing nursing homes, home health, long-term care, health care plans and the miscellaneous institutions discussed in Section 2.14. Based on discussions with industry contacts and consultants, most physicians and the staff at clinics, infusion centers, and pharmacies servicing nursing homes, home health, and longer term care have Internet access and printing capabilities (Health Care Provider C, 2009; Health Care Provider F, 2009; Expert B, 2009). Physicians and clinics receive PI with samples and vaccines. Sometimes a clinic will contract with a pharmacist who is otherwise self-employed or employed at a pharmacy to provide oversight of the clinic's drug dispensing activities. In other settings, the pharmacy might be in the clinic (Expert B, 2009). Drugs and vaccines are not dispensed, but are administered, in clinics.

While some health care plans that are part of a hospital system might make greater use of PI, ERG is unable to identify how many of the 1,058 health care plans operate in this fashion and is thus assuming all are infrequent users. Based on discussions with our pharmacy industry consultant and several industry contacts, ERG concluded that these entities only make sporadic use of PI. ERG initially also considered dentists, nurses, and mail order pharmacies, but after discussions with representatives of these groups, determined that their use of PI is negligible (Health Care Provider E, 2009; Health Care Provider A, 2009; Health Care Provider B, 2009; Pharmacist Association D, 2009; et al.).

ERG projects that infrequent users might print out the PI between four and eight times per year to learn more about new products. Given the infrequency of PI use, the only cost estimated is the material and labor cost of searching for and printing the insert. As before, ERG assumed a cost of 4 cents per page and a 20 to 30 page insert that takes 30 seconds to 1 minute to print.

As discussed in section 2.9, ERG assumes there are 377,123 physicians who would make some use of the PI. Assuming an average hourly wage of $129.17 (MGMA, 2008), ERG estimates a unit annual cost per physician of between $8 and $27 and a total annual cost of between $2.8 million and $10.1 million for all 377,123 physicians the ERG estimates use PI (See Table 6-15). For other users of PI such as pharmacists at nursing homes, home health care providers, long term care facilities, and healthcare plans, and using a blended hourly wage of $67.99, ERG estimates a unit annual cost of between $5 and $19, and a total annual cost of between $0.07 and $0.24 million. Summing costs for physicians and other infrequent users suggests total costs of between $2.9 and $10.4 million (see Table 6-15).

Table 6-15. Infrequent Users – Unit and Total Costs

Printing Costs	Low Estimate	High Estimate	Source
Physicians			
Expected frequency of printing electronic PI annually per physician	4	8	ERG estimate
Cost per page (including ink and paper)	$0.04	$0.04	PCSupportTips.com, 2008; TopTenReviews.com, 2009
Average number of pages per copy of PI	20	30	Manufacturer D, 2009; Pharmacist B, 2009
Average material cost to print one copy of PI	$0.80	$1.20	
Minutes required to print average PI	0.5	1	Pharmacist B, 2009; ERG estimate
Physician wages	$129.17	$129.17	MGMA, 2008

Table 6-15. Infrequent Users – Unit and Total Costs

Printing Costs	Low Estimate	High Estimate	Source
Average labor cost to print one copy of PI	$1.08	$2.15	
Unit annual cost	$8	$27	
Physicians	899,540	899,540	COGME, 2005
Of physicians, percent involved in patient care	94%	94%	COGME, 2005
Of physicians involved in patient care, percent that are not surgeons	89%	89%	BLS, 2007f
Prescribing physicians	754,246	754,246	
Percent of prescribing physicians expected to use PI	50%	50%	ERG estimate
Physicians using PI	377,123	377,123	
Total annual cost	$2,830,562	$10,115,454	
Nursing Homes, Home Health, Long Term Care, Healthcare Plans			
Expected frequency of printing electronic PI annually per year	4	8	ERG estimate
Cost per page (including ink and paper)	$0.04	$0.04	PCSupportTips.com, 2008; TopTenReviews.com, 2009
Average number of pages per copy of PI	20	30	Manufacturer D, 2009; Pharmacist B, 2009
Average material cost to print one copy of PI	$0.80	$1.20	
Minutes required to print average PI	0.5	1	Pharmacist B, 2009; ERG estimate
Pharmacist wage (25% director of pharmacy/75% staff pharmacist)	$67.99	$67.99	BLS, 2007a
Average labor cost to print one copy of PI	$0.57	$1.13	
Unit cost per pharmacist	$5	$19	
Number of pharmacists per pharmacy	1	1	ERG estimate
Unit annual cost	$5	$19	
Nursing home/home health/long term care facilities	4,514	4,514	HDMA, 2008
Healthcare plan pharmacies	1,058	1,058	HDMA, 2008
Miscellaneous institutions	7,153	7,153	HDMA, 2008
Total annual cost	$69,558	$237,511	
Total Costs for All Infrequent Users	**$2,900,120**	**$10,352,964**	

6.1.6 Manufacturers

Label Changes

Manufacturers will incur a cost to add text to the immediate container labeling and outer container labeling to provide a toll free number and a reference to the URL where the PI can be found on the Internet (e.g., the Internet address of an FDA Web Portal).

Some label change costs will be accrued on a per-firm basis. To make label changes, a manufacturer's regulatory affairs officers typically hold a meeting to review the proposed regulation and determine what labeling changes need to be made. Given that the labeling change required by the proposed regulation is the same or similar for all products, ERG judged that one meeting would be held that would cover all products. Based on previous studies completed by ERG on pharmaceutical labeling changes and conversations with industry experts, ERG estimates that small and medium and generic companies would conduct an eight hour meeting and that large companies would meet for 10 hours (ERG, 2002; Industry Expert A). The Bureau of Labor Statistics (2007e) suggests that regulatory affairs staff hourly wages average $42.41. However this will vary by manufacturer size, so we assume an hourly wage of $35 for regulatory affairs staff at small and medium manufacturers, $50 at large manufacturers, and $40 at generic manufacturers (Expert A, 2009). Label changes will also require coordination between several departments. ERG estimates that this will require 16 hours of meetings for small, medium, and generic firms, and 20 hours for large firms. ERG uses an average managerial wage for all staff members involved in these interdepartmental meetings of $70.57 per hour for small and medium firms (BLS 2008c). Applying the same ratio of wage differentials as used in the case of regulatory affairs officers (Expert A, 2009) suggests managerial wages of $100.82 for large brand manufacturers, $70.57 for small and medium brand manufacturers, and $80.65 for generic manufacturers. Together, these meetings will cost $1,409 for small and medium brand manufacturers, $2,516 for large brand manufacturers, and $1,610 for generic manufacturers.

Other label change costs will be accrued on a per-SKU basis, including manufacturing hours required to make changes on the production line, the cost for new artwork and printing plates, and inventory loss. These per-SKU costs assume that 30 to 40 percent of SKUs have both primary labeling and outer carton labeling that will need to be changed[5]. Manufacturing hours to make changes on the production line to accommodate the new labeling will vary by company size. Based on ERG's 2002 Pharmaceutical Labeling Model, ERG estimates that manufacturing hours required for the proposed labeling change would be six hours for small, medium, and generic companies (ERG, 2002). Large companies would require 20 hours per SKU given the greater complexity of their operations. With respect to artwork, printing plates generally cost about $300 per plate. Each SKU will require a new plate and each level of packaging (inner and outer) will need a new plate. Despite the growth in digital printing, printing with plates is still considered the most cost-effective in the prescription drug industry. Prescription drug labels are generally not very complex, hence the low cost.

Inventory loss is generally dependent on the time allowed to comply with a proposed rule. Given that pharmaceutical companies generally do not keep more than a few months worth of inventory on hand, these costs can be reduced significantly with an implementation period of two years or more. However, even though manufacturers can make every effort to reduce inventory loss, there is some minimum loss that will always occur due to challenges in coordinating various timelines in production. ERG estimated an average irreducible container inventory loss cost of $300 for small, medium, and generic companies and $750 for large companies and an average irreducible carton inventory loss cost of $1,000 for small, medium, and generic companies and $2,500 for large companies (ERG, 2002).

[5] The estimate was provided by FDA and based on Orange Book data that roughly 60 percent of products have solid dosage forms. Solid dosage forms usually only have one label on the immediate container and no carton. Based on this data, FDA assumed that 40 percent of SKUs have an outer carton. Furthermore, FDA also assumed that 40 percent is an upper bound on the number of SKUs with cartons because the original estimate is based on a count of products and there exist many more SKUs than products with solid dosage forms. Only secondary containers that the customer might see are considered, not shipping containers.

For those manufacturing SKUs with an inner container only, small and medium manufacturers are expected to incur a one-time, per SKU unit labeling cost of $726, large manufacturers are expected to incur a cost of $1,590 per SKU, and generic manufacturers are expected to incur a cost of $750. For those manufacturing SKUs with an inner and outer container, small and medium manufacturers are expected to incur a one-time, per SKU unit labeling cost of $2,026, large manufacturers are expected to incur a cost of $4,390 per SKU, and generic manufacturers are expected to incur a cost of $2,050. Total one-time label change costs are estimated at between $8.6 million and $15.9 million for small and medium brand manufacturers, between $18.6 million and $34.4 million for large brand manufacturers, and between $17.5 million and $32.2 million for generic manufacturers (see Table 6-16).

Non-standard Label Costs

ERG also considered that some manufacturers will not be able to add the additional required labeling information due to size constraints on small packages. Such manufacturers will need to modify their labeling and/or packaging formats in order to provide the information, and these costs are added onto standard label change costs. To accommodate such eventualities, ERG judged that 10 to 15 percent of SKUs would have some type of constraint in making the required labeling change. Based on previous responses by manufacturers to a lack of space for new text on pharmaceutical labeling, ERG assumed that the most likely response to manufacturers to space constrains would be to use a non-standard label, such as a peel back or accordion label (ERG, 2002). These labels fold out as several labeling panels, thus providing more labeling area for new text. Non-standard labels will require additional time to create. ERG estimated eight hours of additional regulatory affairs time for small, medium and generic companies and 16 hours for large companies. Additional artwork (at $300 per SKU) will also be necessary for the extra labeling panels. Labeling machines will need to be adjusted in order to print the non-standard label. Based on ERG's 2002 labeling model, ERG estimated $2,500 to $2,850 for the capital cost to adjust the labeler equipment, along with an engineering cost equal to 25 percent of the capital costs (ERG, 2002). This generates a unit one-time cost of $3,705 for small and medium manufacturers, $4,663 for large manufacturers, and $3,745 for generic manufacturers. Non-standard labels also cost more than the average label. ERG estimated an additional cost of three cents per label for small and medium companies and two cents per label for large and generic companies (ERG, 2002). This results in an annual unit cost of between $300 and $600 for small and medium brand manufacturers, between $1,000 and $1,500 for large brand manufacturers, and between $600 and $800 for generic manufacturers.

Total one-time costs for non-standard labels are estimated at between $2.8 million and $6.9 million for small brand manufacturers, between $3.5 million and $8.7 million for large brand manufacturers, and between $5.6 million and $14 million for generic manufacturers. Total annual costs for non-standard labels are estimated at between $0.2 million and $1.1 million for small brand manufacturers, between $0.8 million and $2.8 million for large brand manufacturers, and between $0.9 million and $3 million for generic manufacturers (see Table 6-16).

Toll Free Number

Manufacturers will be required to maintain a toll free number that pharmacists or other PI users can call if they do not have Internet access. ERG assumed that manufacturers will use existing phone infrastructure but will need to add an option so that someone can request that PI of a product be mailed or faxed to them. Based on a small sample of old toll free numbers used by pharmaceutical manufacturers, most of which have not changed to date, we also assume that manufacturers will not change the number frequently. Any change in number would result in printed materials containing the phone number being misbranded. This will result in labor costs to modify the phone system, as well as to address requests. The cost of modifications to the phone systems is judged to be negligible. With respect to ongoing costs, ERG projects that small and medium companies may get approximately five to 10 requests per month, while

larger companies are likely to receive 50 to 150 and generic companies 10 to 20 (Expert A, 2009). The Bureau of Labor Statistics (2007f) estimates a loaded hourly wage for staffing these phone lines of $14.86, but this will likely vary with establishment size (Expert A, 2009). Accordingly, ERG estimates loaded hourly wages for phone staff of $15 for small and medium companies, $18 for large companies and $16 for generic companies. ERG assumes that half of firms will use automated phone systems instead of operators, and that this cuts the costs of maintaining a toll free number in half. This results in a minimal average per firm cost of between $9 and $16 per year for small brand manufacturers, between $113 and $338 for large manufacturers, and between $20 and $40 for generic manufacturers. For all firms, total annual costs are $1,525 to $3,881 for small and medium brand manufacturers, $17,533 to $66,946 for large manufacturers, and $4,630 to $11,786 for generic manufacturers (see Table 6-16).

Medication Guides and other PPIs

Because Medication Guides, where required, are often appended to the professional prescribing information portion of the PI (FDA, 2007), it is possible that some manufacturers will have to reformat the labeling. However, there are several reasons to believe that the cost impacts of this change will be negligible. Some manufacturers, such as Eli Lilly, report that they already provide Medication Guides separately (FDA, 2007), and ERG's survey of PI indicates that while most Medication Guides are available appended to the end of the PI, in the vast majority of cases the Medication Guide is already available separately as well. Finally, ERG's conversations with industry representatives indicate that having to produce the Medication Guide separately would not incur any costs (Manufacturer A, 2009).

6.1.7 Repackagers

Label Change Costs

Like manufacturers, repackagers (a category which for this analysis also includes repackagers and private label distributors) will incur costs to make label changes to alter primary and secondary containers and other labeling to accommodate new text required by the proposed rule. While it is estimated for manufacturers that 30 to 40 percent of SKUs have outer containers, this estimate was reduced for repackagers to reflect that repackaged drugs are usually sold as solid dosage forms and thus are much less likely to have an outer container. FDA estimates that 5 to 15 percent of repackaged SKUs have an outer container (carton). ERG estimates that labeling changes will require four hours of regulatory affairs meetings per firm. At an hourly wage for regulatory affairs officers of $35, this totals $140 per firm. Because repackagers are largely reproducing content from manufacturers and have less interest in market position, we assume that there will be no interdepartmental meetings. Labeling change costs accrued on a per-SKU basis will be similar to those accrued by manufacturers, except we estimate that repackagers will require only four manufacturing hours per SKU due to using less equipment than manufacturers. Accounting for production, artwork, and inventory loss results in unit one-time costs of $684 for SKUs with an inner container only and $1,984 for SKUs with an inner and outer container. Total one-time costs range between $90.0 and $132.0 million (see Table 6-17).

Non-Standard Label Costs

Repackagers will incur additional costs similar to manufacturers in producing non-standard labels in instances where small packages will not accommodate the required text. ERG estimates that generating non-standard labels will require an additional four hours of regulatory affairs meetings per firm, additional artwork costs of $300 per SKU, capital costs of $2,500 for adjusting labeling equipment along with 25 percent of capital costs for engineering adjustments. This suggests unit one-time costs of $3,705 per firm. At a cost per peel back label of $0.03 and between 10,000 and 20,000 copies of the labels produced per SKU, this suggest unit annual costs of $300 to $600. Assuming that between 10 and 15

percent of labels cannot accommodate the proposed text results in total one-time costs of $44.5 million to $83.4 million and total annual costs of $3.6 million to $13.5 million (see Table 6-17).

Table 6-16. Prescription Drug and Biological Manufacturers – Unit and Total Costs

	Small/Medium Brand Manufacturers		Large Brand Manufacturers		Generic Manufacturers		Source
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate	
Label Change Costs (per Firm)							
Hours for regulatory affairs meeting	8	8	10	10	8	8	Expert A, 2009; ERG estimate
Regulatory affairs wage rate/hr	$35.00	$35.00	$50.00	$50.00	$40.00	$40.00	BLS, 2007d; Expert A, 2009
Hours for interdepartmental and subdepartmental meetings	16	16	20	20	16	16	ERG estimate
Professional wage rate/hr	$70.57	$70.57	$100.82	$100.82	$80.65	$80.65	BLS, 2008c
Unit one-time cost	$1,409	$1,409	$2,516	$2,516	$1,610	$1,610	
Label Change Costs (per SKU)							
Manufacturing hours	6	6	20	20	6	6	ERG, 2002
Production worker wage rate ($/hr)	$21.00	$21.00	$27.00	$27.00	$25.00	$25.00	BLS, 2007d; Expert A, 2009
Immediate container							
Artwork	$300	$300	$300	$300	$300	$300	ERG, 2002
Container label inventory loss (irreducible minimum)	$300	$300	$750	$750	$300	$300	ERG, 2002
Outer container							
Artwork	$300	$300	$300	$300	$300	$300	ERG, 2002
Carton label inventory loss (irreducible minimum)	$1,000	$1,000	$2,500	$2,500	$1,000	$1,000	ERG, 2002

Table 6-16. Prescription Drug and Biological Manufacturers – Unit and Total Costs

	Small/Medium Brand Manufacturers		Large Brand Manufacturers		Generic Manufacturers		Source
Unit one-time cost for inner container only	$726	$726	$1,590	$1,590	$750	$750	
Additional unit one-time cost for outer container	$1,300	$1,300	$2,800	$2,800	$1,300	$1,300	
Number of firms	163	207	156	198	232	295	ERG, 2008
Number of SKUs with inner AND outer containers	2,250	5,000	2,250	5,000	4,500	10,000	FDA estimate
Total number of SKUs	7,500	12,500	7,500	12,500	15,000	25,000	ERG, 2002
Total one-time costs	$8,599,164	$15,866,663	$18,617,171	$34,374,126	$17,472,846	$32,224,532	
Additional Cost of Adding a Non-standard Label (Leaflet) for Small Package Sizes (per SKU)							
Additional hours of regulatory affairs input per SKU	8	8	16	16	8	8	ERG estimate
Regulatory affairs labor wage rate ($ per hour)	$35.00	$35.00	$50.00	$50.00	$40.00	$40.00	BLS, 2007d; Expert A, 2009
Additional artwork cost per SKU	$300	$300	$300	$300	$300	$300	ERG, 2002
Capital cost of adjusting labeler (parts, labor)	$2,500	$2,500	$2,850	$2,850	$2,500	$2,500	ERG, 2002
Engineering costs of adjustments (25% of capital costs)	$625	$625	$713	$713	$625	$625	
Unit one-time cost	$3,705	$3,705	$4,663	$4,663	$3,745	$3,745	
Cost of a peel back label	$0.03	$0.03	$0.02	$0.02	$0.02	$0.02	ERG, 2002
Units per SKU	10,000	20,000	50,000	75,000	30,000	40,000	ERG estimate
Unit annual cost	$300	$600	$1,000	$1,500	$600	$800	
Percentage of SKUs that cannot accommodate proposed text	10%	15%	10%	15%	10%	15%	ERG estimate
Number of SKUs that cannot accommodate proposed text	750	1,875	750	1,875	1,500	3,750	ERG, 2002
Total one-time costs	$2,778,750	$6,946,875	$3,496,875	$8,742,188	$5,617,500	$14,043,750	
Total annual costs	$225,000	$1,125,000	$750,000	$2,812,500	$900,000	$3,000,000	

Table 6-16. Prescription Drug and Biological Manufacturers – Unit and Total Costs

	Small/Medium Brand Manufacturers		Large Brand Manufacturers		Generic Manufacturers		Source
Toll Free Number Costs (per Firm)							
Number of calls per month	5	10	50	150	10	20	Expert A, 2009; ERG estimate
Switchboard operator hours	0.8	1.7	8.3	25.0	1.7	3.3	ERG estimate
Wage rate	$15.00	$15.00	$18.00	$18.00	$16.00	$16.00	BLS, 2007e; Expert A, 2009
Savings using automation versus switchboard	50%	50%	50%	50%	50%	50%	
Unit annual cost	$9	$19	$113	$338	$20	$40	
Number of firms	163	207	156	198	232	295	FDA estimate
Total annual costs	$1,525	$3,881	$17,533	$66,946	$4,630	$11,786	

Toll Free Number Costs

Repackagers will also be required to maintain a toll free number for those who cannot access the PI electronically. We assume that they will not change the number often, as that would result in printed materials containing the phone number being misbranded. However, not all the entities in our repackager analysis will have to provide a toll free number. In the case of private label distributors, only the firm that attaches the label will be the one responsible for providing a toll free number. Thus one contract manufacturer can maintain a single toll free number for multiple private labels. To account for this, we assume that only one third of the total number of repackagers will have to maintain a toll free number. We further assume that repackagers would receive five to 10 calls per month (Expert A, 2009), requiring 0.8 to 1.7 hours for a switchboard operator at an average hourly wage of $15 (BLS, 2007e; Expert A, 2009). We also assume that using an automated answering system reduces costs by 50 percent and that half of repackagers will use automated systems. This assumption results in unit annual costs of $9 to $19 per firm, and total annual costs of $2,813 to $8,125 for all repackaging firms (see Table 6-17).

Table 6-17. Repackagers – Unit and Total Costs

Cost	Low Estimate	High Estimate	Source
Label Change Costs (per Firm)			
Hours for regulatory affairs meeting	4	4	Expert A, 2009; ERG estimate
Regulatory affairs wage rate/hr	$35.00	$35.00	BLS, 2007d; Expert A, 2009
Unit one-time cost	$140	$140	
Label Change Costs (per SKU)			
Manufacturing hours	4	4	ERG, 2002
Production worker wage rate ($/hr)	$21.00	$21.00	BLS, 2007d; Expert A, 2009
Immediate container			
Artwork	$300	$300	ERG, 2002
Container label inventory loss (irreducible minimum)	$300	$300	ERG, 2002
Outer container			
Artwork	$300	$300	ERG, 2002
Carton label inventory loss (irreducible minimum)	$1,000	$1,000	ERG, 2002
Unit one-time cost for inner container only	$684	$684	
Additional unit one-time cost for outer container	$1,384	$1,384	
Number of firms	900	1,300	FDA estimate
Number of SKUs with inner AND outer containers	6,000	22,500	FDA estimate
Number of SKUs	120,000	150,000	FDA estimate
Total one-time costs	$90,006,000	$132,032,000	
Additional Cost of Adding a Non-standard Label (Leaflet) for Small Package Sizes (per SKU)			
Additional hours of regulatory affairs input per SKU	4	4	ERG estimate
Regulatory affairs labor wage rate ($ per hour)	$35.00	$35.00	BLS, 2007d

Table 6-17. Repackagers – Unit and Total Costs

Cost	Low Estimate	High Estimate	Source
Additional artwork cost per SKU	$300	$300	ERG, 2002
Capital cost of adjusting labeler (parts, labor)	$2,500	$2,500	ERG, 2002
Engineering costs of adjustments (25% of capital costs)	$625	$625	
Unit one-time cost	$3,565	$3,565	
Cost of a peel back label	$0.03	$0.03	ERG, 2002
Units per SKU	10,000	20,000	ERG estimate
Unit annual cost	$300	$600	
Percentage of SKUs that cannot accommodate proposed text	10%	15%	ERG estimate
Number of SKUs that cannot accommodate proposed text	12,000	22,500	
Total one-time costs	$42,780,000	$80,212,500	
Total annual costs	$3,600,000	$13,500,000	
Toll Free Number Costs (per Firm)			
Number of calls per month	5	10	Expert A, 2009; ERG estimate
Switchboard operator hours	0.8	1.7	ERG estimate
Wage rate	$15.00	$15.00	BLS, 2007e; Expert A, 2009
Savings using automation versus switchboard	50%	50%	
Unit annual cost	$9	$19	
Number of firms	300	433	FDA estimate
Total annual costs	$2,813	$8,125	

6.1.8 SPL Submissions

Section 224 of the Food and Drug Administration Amendments Act of 2007, which amends section 510(p) of the Act, expressly requires drug listing information be submitted by electronic means by June 1, 2009. This provision extends the requirement for electronically submitting labeling in SPL format to contract manufacturers[6], repackagers and relabelers; however they may wait to submit the label until there is a change made to the labeling This proposed rule will require all PIs to be submitted within six months after the final rule publishes regardless of whether there was a change made. We assume that the labeling for products subject to 21 CFR 201.100(d)(3) is already being submitted in SPL in accordance with the requirement, and only estimate costs for converting the PIs for unapproved, repackaged, relabeled, or private label products.

Based on data provided by FDA, we estimate that between 20,000 and 25,000 units of PI would have to be converted to SPL under the proposed rule. In order to estimate the cost impact of different

[6] Contract manufacturers list the products made for private label distribution, as part of listing they will be required to submit the PI electronically for each listed product distributed via private label.

compliance timelines for manufacturer submissions of labeling in SPL, ERG spoke with providers of SPL conversion services. Industry sources suggest conversion costs per copy of the PI of $400 (Data Conversion Service Provider A, 2009), and ERG estimates that the process would require an additional 10 hours of quality assurance and validation at a manager-level wage rate of $76.51 per hour, including benefits (BLS, 2008a; BLS, 2008b) (see Table 6-18).

In order to estimate costs under the baseline six-month compliance timeframe, ERG first estimated the unit and total costs that manufacturers and repackagers would incur if they submitted their labeling in SPL given a two-year compliance period. These costs are listed in Tables 6-18 and 6-19 and considered again in Section 8 as the regulatory alternative.

In order to account for the potential for higher charges by SPL vendors due to rush fees or overtime costs for the 6 month compliance timeframe, we applied a 20 percent cost premium to the 2-year compliance time costs. While the data service conversion provider with whom we spoke did not anticipate capacity constraints nor rush fees for production times in these circumstances (Data Conversion Service Provider A, 2009), the cost premium accounts for any unforeseen cost increases on the part of manufacturers or data conversion service providers. If complications do arise, data conversion service providers would respond by working overtime or shifting staff from projects with greater deadline flexibility. Increasing automation will also increase capacity. The six-month implementation cost in Table 6-19 reflects the two-year cost adjusted with the 20 percent premium.

Next, we calculated the present value of the regulatory costs because manufacturers and repackagers would incur the regulatory cost earlier than the two-year time frame upon which the costs are based. ERG used discounting factors (0.94 and 0.87 for 3 and 7 percent discount rate, respectively) to calculate the present value of this cost7 (EPA, Undated). This calculation results in total one-time costs for submitting SPL within six months of $13.1 million to $16.5 million at a 3 percent discount rate and $12.1 million to $15.3 million at a 7 percent discount rate (see Table 6-20).

6.1.9 Impact on Paper and Printing Industries

The proposed regulation will sharply reduce demand for the specialized paper used in printing of PI, and for the printing function itself. Because of the unique features of PI paper and of the printing and folding processes, a small, specialized industry has grown around the provision of PI services to the pharmaceutical industry. This specialization, however, limits the affected firms' ability to avoid the economic impacts of the fall in demand for printed PI.

Three paper companies (Fraser, Boise, and Domtar) produce the lightweight paper used in PI. Of these, Fraser and Domtar are Canadian-owned companies that operate mills in the United States. Boise is one of the largest paper producers in the world, with a diverse range of production operations. The reduction in thin-paper demand caused by eliminating paper PI would most likely not result in the closing of a thin-paper mill in the U.S., but rather could result in the loss of 100-200 jobs at the companies the produce and distribute thin paper. It would also contribute to the ongoing economic decline of thin paper manufacturing due to reduced demand for paper-based medical, financial, and government reporting (Paper Manufacturer B, 2009). There are 40 to 50 printing companies specialized to varying degrees in PI

[7] These numbers are obtained from the present value formula, $PV = \frac{C}{(1+r)^t}$, where C is the number of monetary units, r is the interest or discount rate, and t is the number of time periods. Letting $C = 1$, $r = 0.03$ or 0.07, and $t = 2$, we obtain 0.942595909, which we round to 0.94, and 0.873438728, which we round to 0.87.

work. With the end of the requirement for a paper version of the PI, the market for this work will virtually end.

Table 6-18. Unit SPL Costs for Unapproved and Repackaged Drugs

	Unique Non-Applicant PIs to be Converted [a]		Number of Firms Affected		Labor Hours	Unit Cost
	Low Estimate	High Estimate	Low Estimate	High Estimate		
Initial conversion	20,000	25,000	NA	NA	NA	$400
QA review of converted file	20,000	25,000	NA	NA	2	$153
Cost to validate new SPL submission process	NA	NA	900	1,300	8	$612

[a] FDA supplied estimate. We assume that in the absence of the regulation, those affected would have incurred the costs two years later.

Table 6-19. Total SPL Costs for Unapproved and Repackaged Drugs

	2-Year Implementation Total Cost		6 Month Implementation Total Cost	
	Low Estimate	High Estimate	Low Estimate	High Estimate
Initial conversion	$8,000,000	$10,000,000	$9,600,000	$12,000,000
QA review of converted file	$3,060,264	$3,825,330	$3,672,317	$4,590,396
Cost to validate new SPL submission process	$550,448	$795,669	$661,017	$954,802
Total one-time cost	**$11,611,112**	**$14,620,999**	**$13,933,334**	**$17,545,198**

Table 6-20. 6 Month Implementation Total Cost (Present Value)

	3% Discount Factor		7% Discount Factor	
	Low Estimate	High Estimate	Low Estimate	High Estimate
Initial conversion	$9,024,000	$11,280,000	$8,352,000	$10,440,000
QA review of converted file	$3,451,978	$4,314,972	$3,194,916	$3,993,645
Cost to validate new SPL submission process	$621,356	$897,514	$575,085	$830,678
Total one-time cost	**$13,097,334**	**$16,492,486**	**$12,122,000**	**$15,264,323**

As noted in the discussion above, the printing companies use either sheet-fed or web printing processes. The sheet fed system can be more readily adapted to other non-package-insert tasks. But that share of the industry is reported in 2009 to have excess capacity. The web printing machinery is less readily adaptable to other non-package-insert tasks. Thus, the market forecast is poor for companies using either printing process. Numerous business failures among this group of printing companies appear likely. One printer estimated that 40-45 percent of pharmaceutical printing plants would close.

6.2 ANNUALIZED COMPLIANCE COSTS

The costs to manufacturers, repackagers, pharmacies, and infrequent users of PI discussed above are summarized in the tables below. The annualized costs tables present one-time and annual costs and the annualized one-time costs with a 3 percent and 7 percent discount rate and assuming a two-year compliance period. Annualized one-time and annual costs are then added together to obtain total annualized costs. Annualized costs that accrue to PI users and manufacturers are summed to generate total impacts on pharmacies and manufacturers.

Table 6-21 summarizes the total impacts of the proposed regulation on users of PI, manufacturers, users of PI, assuming two-year compliance time for converting to electronic PIs and six months compliance time for submitting labeling in SPL. The proposed regulation results total costs of between $75.5 million and $148.8 million at a 3 percent discount rate, and between $80.8 million and $157.8 million at a 7 percent discount rate.

Table 6-21. Total Annualized Compliance Costs of the Proposed Regulation

	3% Discount Rate		7% Discount Rate	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**
2-Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$8,531,861	$20,173,157	$9,954,736	$22,994,603
Repackagers	$19,169,383	$38,389,655	$22,508,552	$43,726,967
Total Costs (without SPL costs)	$73,957,443	$146,819,255	$78,900,907	$155,448,696
Total Costs (with 6 month SPL implementation)	**$75,492,850**	**$148,752,677**	**$80,765,672**	**$157,796,855**

6.2.1 Pharmacies and Infrequent Users of PI

As a result of the proposed regulation and assuming a 7 percent discount rate, ERG estimates that chain pharmacies will incur total annualized costs of between $20.6 million and $36.9 million, independent pharmacies will incur total annualized costs of between $9 million and $16.1 million, hospital pharmacies will incur total annualized costs of between $13.9 million and $25.4 million, and infrequent users of PI will incur total annualized costs of between $2.9 million and $10.4 million. All pharmacies' and infrequent users' annualized costs sum to between $46.4 million and $88.7 million (see Table 6-22).

Assuming a 3 percent discount rate, ERG estimates that chain pharmacies will incur total annualized costs of between $20.5 million and $36.7 million, independent pharmacies will incur total annualized costs of between $9 million and $16 million, hospital pharmacies will incur total annualized costs of between $13.9 million and $25.2 million, and infrequent users of PI will incur total annualized

costs of between $2.9 million and $10.4 million. All pharmacies' and infrequent users' annualized costs sum to between $46.3 million and $88.3 million (see Table 6-23).

In both cases, the bulk of these costs result from anticipated delays in accessing and printing PI and the cost of printing.

6.2.2 Manufacturers

Label change costs are a one-time cost. At a 7 percent discount rate, small and medium brand manufacturers will have total annualized label change costs of between $1.2 million and $2.3 million, large brand manufacturers will have total annualized costs of between $2.7 million and $4.9 million, and generic manufacturers will have total annualized costs of between $2.5 million and $4.6 million. Summing these costs across manufacturers, total annualized label change costs will be between $6.4 million and $11.7 million (see Table 6-24).

At a 3 percent discount rate, small and medium brand manufacturers will have total annualized label change costs of between $1.0 million and $1.9 million, large brand manufacturers will have total annualized costs of between $2.2 million and $4.0 million, and generic manufacturers will have total annualized costs of between $2.0 million and $3.8 million. Summing these costs across manufacturers, total annualized label change costs will be between $5.2 million and $9.7 million (see Table 6-25).

Producing non-standard labeling for small packages that can't accommodate new text will involve one-time costs. Annualizing these costs at a 7 percent discount rate, small and medium brand manufacturers will have total annualized costs of between $0.6 million and $2.1 million, large brand manufacturers will have total annualized costs of between $1.2 million and $4.1 million, and generic manufacturers will have total annualized costs of between $1.7 million and $5 million. Summing these costs across manufacturers, total annualized label change costs will be between $3.6 million and $11.2 million (see Table 6-24).

Annualizing non-standard labeling costs at a 3 percent discount rate, small and medium brand manufacturers will have total annualized costs for non-standard labeling of between $0.6 million and $1.9 million, large brand manufacturers will have total annualized costs of between $1.2 million and $3.8 million, and generic manufacturers will have total annualized costs of between $1.6 million and $4.6 million. Summing these costs across manufacturers, total annualized costs for non-standard labeling will be between $3.3 million and $10.4 million (see Table 6-25).

Under our assumption that firms will be able to use their existing infrastructure to maintain a toll free number, that maintenance is an annual cost that is not annualized. As noted in section 6.1.6 above, total annual costs of maintaining a toll free number are $1,525 to $3,881 for small and medium brand manufacturers, $17,533 to $66,946 for large brand manufacturers, and between $4,630 and $11,786 for generic manufacturers. Summing these costs across manufacturers, total annualized costs for maintaining a toll free number are between $23,688 and $82,613 (see Table 6-24 and Table 6-25).

Table 6-22. Pharmacies and Infrequent Users of PI – Annualized Compliance Costs (7 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate
Chain Pharmacy								
Internet access	$0	$0	$0	$0	$10,043	$26,781	$10,043	$26,781
Delays	$0	$0	$0	$0	$15,350,920	$19,188,650	$15,350,920	$19,188,650
Printing	$0	$0	$0	$0	$4,628,382	$15,804,010	$4,628,382	$15,804,010
Computer hardware/operating and maintenance	$1,431,715	$5,378,605	$203,844	$765,792	$143,172	$537,861	$347,016	$1,303,653
Training	$1,973,058	$3,946,117	$280,919	$561,838	$0	$0	$280,919	$561,838
Total	$3,404,773	$9,324,722	$484,763	$1,327,631	$20,132,516	$35,557,301	$20,617,279	$36,884,932
Independent Pharmacy								
Internet access	$0	$0	$0	$0	NA	NA	$0	$0
Delays	$0	$0	$0	$0	$6,712,829	$8,391,036	$6,712,829	$8,391,036
Printing	$0	$0	$0	$0	$2,023,953	$6,910,962	$2,023,953	$6,910,962
Computer hardware/operating and maintenance	$626,077	$2,352,019	$89,139	$334,875	$62,608	$235,202	$151,747	$570,076
Training	$862,802	$1,725,604	$122,844	$245,687	$0	$0	$122,844	$245,687
Total	$1,488,879	$4,077,623	$211,983	$580,562	$8,799,389	$15,537,199	$9,011,372	$16,117,761
Hospital Pharmacy								
Internet access	$0	$0	$0	$0	$826,000	$2,202,667	$826,000	$2,202,667
Delays	$0	$0	$0	$0	$9,768,761	$12,210,951	$9,768,761	$12,210,951
Printing	$0	$0	$0	$0	$2,945,332	$10,057,091	$2,945,332	$10,057,091
Computer hardware/operating and maintenance	$383,394	$1,440,318	$54,587	$205,069	$38,339	$144,032	$92,926	$349,101
Training	$1,937,314	$3,874,629	$275,830	$551,660	$0	$0	$275,830	$551,660
Total	$2,320,708	$5,314,947	$330,417	$756,729	$13,578,432	$24,614,740	$13,908,849	$25,371,469
Infrequent Users								
Printing	$0	$0	$0	$0	$2,900,120	$10,352,964	$2,900,120	$10,352,964
Total for All Users of PI	**$7,214,360**	**$18,717,291**	**$1,027,163**	**$2,664,921**	**$45,410,456**	**$86,062,205**	**$46,437,619**	**$88,727,126**

Table 6-23. Pharmacies and Infrequent Users of PI – Annualized Compliance Costs (3 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate
Chain Pharmacy								
Internet access	$0	$0	$0	$0	$10,043	$26,781	$10,043	$26,781
Delays	$0	$0	$0	$0	$15,350,920	$19,188,650	$15,350,920	$19,188,650
Printing	$0	$0	$0	$0	$4,628,382	$15,804,010	$4,628,382	$15,804,010
Computer hardware/operating and maintenance	$1,431,715	$5,378,605	$167,841	$630,537	$143,172	$537,861	$311,012	$1,168,397
Training	$1,973,058	$3,946,117	$231,303	$462,605	$0	$0	$231,303	$462,605
Total	$3,404,773	$9,324,722	$399,143	$1,093,142	$20,132,516	$35,557,301	$20,531,659	$36,650,443
Independent Pharmacy								
Internet access	$0	$0	$0	$0	NA	NA	$0	$0
Delays	$0	$0	$0	$0	$6,712,829	$8,391,036	$6,712,829	$8,391,036
Printing	$0	$0	$0	$0	$2,023,953	$6,910,962	$2,023,953	$6,910,962
Computer hardware/operating and maintenance	$626,077	$2,352,019	$73,395	$275,728	$62,608	$235,202	$136,003	$510,930
Training	$862,802	$1,725,604	$101,147	$202,293	$0	$0	$101,147	$202,293
Total	$1,488,879	$4,077,623	$174,542	$478,022	$8,799,389	$15,537,199	$8,973,931	$16,015,221
Hospital Pharmacy								
Internet access	$0	$0	$0	$0	$826,000	$2,202,667	$826,000	$2,202,667
Delays	$0	$0	$0	$0	$9,768,761	$12,210,951	$9,768,761	$12,210,951
Printing	$0	$0	$0	$0	$2,945,332	$10,057,091	$2,945,332	$10,057,091
Computer hardware/operating and maintenance	$383,394	$1,440,318	$44,945	$168,849	$38,339	$144,032	$83,285	$312,881
Training	$1,937,314	$3,874,629	$227,112	$454,225	$0	$0	$227,112	$454,225
Total	$2,320,708	$5,314,947	$272,058	$623,074	$13,578,432	$24,614,740	$13,850,490	$25,237,814
Infrequent Users								
Printing	$0	$0	$0	$0	$2,900,120	$10,352,964	$2,900,120	$10,352,964
Total for all users of PI	**$7,214,360**	**$18,717,291**	**$845,743**	**$2,194,238**	**$45,410,456**	**$86,062,205**	**$46,256,200**	**$88,256,442**

Summing costs annualized at a 7 percent discount rate results in total annualized costs for small and medium brand manufacturers of between $1.8 and $4.4 million, costs for large brand manufacturers of between $3.9 million and $9.0 million, costs for generic manufacturers of between $4.2 million and $9.6 million, and costs for all manufacturers of between $10.0 million and $23.0 million (see Table 6-24).

Summing costs annualized at a 3 percent discount rate results in total annualized costs for small and medium brand manufacturers of between $1.6 million and $3.8 million, costs for large brand manufacturers of between $3.4 million and $8.0 million, costs for generic manufacturers of between $3.6 million and $8.4 million, and costs for all manufacturers of between $8.5 million and $20.2 million (see Table 6-25).

6.2.3 Repackagers

Label change costs are a one-time cost for repackagers. Annualizing label change costs at a 7 percent discount rate produces total annualized costs of between $12.8 million and $18.8 million (see Table 6-26). Annualizing label change costs at a 3 percent discount rate produces annualized costs of between $10.6 million and $15.5 million (see Table 6-27).

Producing non-standard labels for small package sizes that can't accommodate the proposed text will also involve one-time costs for repackagers. Annualizing non-standard labeling costs at a 7 percent discount rate, total annualized costs will between $9.7 million and $24.9 million (see Table 6-26). Annualizing non-standard-labeling costs at a 3 percent discount rate, total annualized costs will be between $8.6 million and $22.9 million (see Table 6-25).

Under our assumption that repackagers will largely use existing infrastructure to maintain a toll free number, there are no one-time costs and so toll free number costs are not annualized. As noted in section 6.1.7 above, total annual costs for maintaining a toll free number are $2,813 to $8,125 for all repackaging firms.

Summing these costs results in total annualized costs for repackagers of between $22.5 million and $43.7 million at a 7 percent discount rate, and between $19.2 million and $38.4 million at a 3 percent discount rate.

Table 6-24. Manufacturers – Annualized Compliance Costs (7 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**
Label Change Costs								
Small/medium brand	$8,599,164	$15,866,663	$1,224,328	$2,259,056	$0	$0	$1,224,328	$2,259,056
Large brand	$18,617,171	$34,374,126	$2,650,666	$4,894,102	$0	$0	$2,650,666	$4,894,102
Generic	$17,472,846	$32,224,532	$2,487,740	$4,588,048	$0	$0	$2,487,740	$4,588,048
Total	$44,689,181	$82,465,322	$6,362,734	$11,741,207	$0	$0	$6,362,734	$11,741,207
Non-standard Label Costs								
Small/medium brand	$2,778,750	$6,946,875	$395,631	$989,079	$225,000	$1,125,000	$620,631	$2,114,079
Large brand	$3,496,875	$8,742,188	$497,876	$1,244,691	$750,000	$2,812,500	$1,247,876	$4,057,191
Generic	$5,617,500	$14,043,750	$799,806	$1,999,514	$900,000	$3,000,000	$1,699,806	$4,999,514
Total	$11,893,125	$29,732,813	$1,693,313	$4,233,284	$1,875,000	$6,937,500	$3,568,313	$11,170,784
Toll Free Number Costs								
Small/medium brand	$0	$0	$0	$0	$1,525	$3,881	$1,525	$3,881
Large brand	$0	$0	$0	$0	$17,533	$66,946	$17,533	$66,946
Generic	$0	$0	$0	$0	$4,630	$11,786	$4,630	$11,786
Total	$0	$0	$0	$0	$23,688	$82,613	$23,688	$82,613
Total Costs [a]								
Small/medium brand	$11,377,914	$22,813,538	$1,619,959	$3,248,135	$226,525	$1,128,881	$1,846,484	$4,377,016
Large brand	$22,114,046	$43,116,314	$3,148,543	$6,138,793	$767,533	$2,879,446	$3,916,076	$9,018,239
Generic	$23,090,346	$46,268,282	$3,287,546	$6,587,562	$904,630	$3,011,786	$4,192,176	$9,599,349
Total	**$56,582,306**	**$112,198,134**	**$8,056,047**	**$15,974,490**	**$1,898,688**	**$7,020,113**	**$9,954,736**	**$22,994,603**

[a] Assuming no voluntary costs

Table 6-25. Manufacturers – Annualized Compliance Costs (3 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**
Label change costs								
Small/medium brand	$8,599,164	$15,866,663	$1,008,084	$1,860,057	$0	$0	$1,008,084	$1,860,057
Large brand	$18,617,171	$34,374,126	$2,182,500	$4,029,696	$0	$0	$2,182,500	$4,029,696
Generic	$17,472,846	$32,224,532	$2,048,351	$3,777,698	$0	$0	$2,048,351	$3,777,698
Total	$44,689,181	$82,465,322	$5,238,935	$9,667,451	$0	$0	$5,238,935	$9,667,451
Non-standard Label Costs								
Small/medium brand	$2,778,750	$6,946,875	$325,754	$814,386	$225,000	$1,125,000	$550,754	$1,939,386
Large brand	$3,496,875	$8,742,188	$409,940	$1,024,851	$750,000	$2,812,500	$1,159,940	$3,837,351
Generic	$5,617,500	$14,043,750	$658,542	$1,646,356	$900,000	$3,000,000	$1,558,542	$4,646,356
Total	$11,893,125	$29,732,813	$1,394,237	$3,485,593	$1,875,000	$6,937,500	$3,269,237	$10,423,093
Toll Free Number Costs								
Small/medium brand	$0	$0	$0	$0	$1,525	$3,881	$1,525	$3,881
Large brand	$0	$0	$0	$0	$17,533	$66,946	$17,533	$66,946
Generic	$0	$0	$0	$0	$4,630	$11,786	$4,630	$11,786
Total	$0	$0	$0	$0	$23,688	$82,613	$23,688	$82,613
Total Costs [a]								
Small/medium brand	$11,377,914	$22,813,538	$1,333,839	$2,674,443	$226,525	$1,128,881	$1,560,363	$3,803,324
Large brand	$22,114,046	$43,116,314	$2,592,441	$5,054,547	$767,533	$2,879,446	$3,359,974	$7,933,993
Generic	$23,090,346	$46,268,282	$2,706,893	$5,424,054	$904,630	$3,011,786	$3,611,523	$8,435,841
Total	**$56,582,306**	**$112,198,134**	**$6,633,172**	**$13,153,044**	**$1,898,688**	**$7,020,113**	**$8,531,861**	**$20,173,157**

[a] Assuming no voluntary costs

Table 6-26. Repackagers – Annualized Compliance Costs (7 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**
Label Change Costs	$90,006,000	$132,032,000	$12,814,830	$18,798,386	$0	$0	$12,814,830	$18,798,386
Non-standard Label Costs	$42,780,000	$80,212,500	$6,090,910	$11,420,455	$3,600,000	$13,500,000	$9,690,910	$24,920,455
Toll Free Number Costs	$0	$0	$0	$0	$2,813	$8,125	$2,813	$8,125
Total Costs	**$132,786,000**	**$212,244,500**	**$18,905,739**	**$30,218,842**	**$3,602,813**	**$13,508,125**	**$22,508,552**	**$43,726,967**

Table 6-27. Repackagers – Annualized Compliance Costs (3 percent discount rate)

	One-Time Costs		Annualized One-Time Costs		Annual Costs		Total Annualized Costs	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**	**Low Estimate**	**High Estimate**
Label Change Costs	$90,006,000	$132,032,000	$10,551,449	$15,478,178	$0	$0	$10,551,449	$15,478,178
Non-standard Label Costs	$42,780,000	$80,212,500	$5,015,121	$9,403,352	$3,600,000	$13,500,000	$8,615,121	$22,903,352
Toll Free Number Costs	$0	$0	$0	$0	$2,813	$8,125	$2,813	$8,125
Total Costs	**$132,786,000**	**$212,244,500**	**$15,566,570**	**$24,881,530**	**$3,602,813**	**$13,508,125**	**$19,169,383**	**$38,389,655**

6.2.4 SPL Submission

Annualizing the cost of submitting labels to SPL within six months results in total annualized costs of between $1.9 million and $2.3 million at a seven percent discount rate and between $1.5 million and $1.9 million at a three percent discount rate (see Table 6-28).

Table 6-28. Annualized SPL Submission Costs

	6 Month Implementation Annualized			
	3%		7%	
	Low Estimate	High Estimate	Low Estimate	High Estimate
Initial conversion	$1,057,888	$1,322,360	$1,284,815	$1,606,018
QA review of converted file	$404,677	$505,846	$491,484	$614,355
Cost to validate new SPL submission process	$72,842	$105,216	$88,467	$127,786
Total one-time cost	**$1,535,407**	**$1,933,423**	**$1,864,766**	**$2,348,159**

6.3 FDA WEB PORTAL

The proposed regulation may require FDA to maintain a Web Portal containing PI for all approved pharmaceuticals. ERG estimated costs for the Web Portal, but we have not included them in the industry totals for compliance costs.

Table 6-29 presents the Web Portal cost estimates. We make the following assumptions, based on conversations with experts in the field:

- FDA vendor will design, develop, deploy, and maintain site/database; It will be English only.
- FDA will populate the database based on label sent in from FDA's Electronic Drug Registration and Listing Systems (e-DRLS).
- FDA can run limited reports on status of PIs, change PI status, and change manufacturer status.
- General users can search database by brand name, generic name, or NDC number, and secondarily by PI section; they can search, print, and download PIs.
- Estimate does not include cost of vendor procurement process.
- ERG assumes a $100 hour blended wage for software engineers

Actual PI entry time will be minimal, but associated processes and internal approvals for each entry are accounted for as well As noted in the table, there is little basis for a forecast; We assume a total of 55,000 records, requiring one quarter hour per record, all inclusive. We also assume 10,000 records per year, requiring one quarter hour per record, all inclusive.

ERG judged that the initial Web Portal development would require approximately $1.7 million in one-time development costs. This would include preparation of specifications, web design work, and the principal web site and database development work. This estimate also includes a one-time charge (estimated at $1.4 million) for the population of the database itself. This estimate, which allows one quarter hour per record for an initial 55,000 records) is among the most speculative estimates here and probably conservative. The estimate also includes maintenance requirements and ongoing costs to assimilate new and updated PI as it is submitted to the database. The ongoing operation and maintenance costs, assuming 10,000 records per year and one quarter hour per record, are estimated at $0.3 million per year. The estimates do not include costs to link the database to any other FDA systems or to generate any additional data or reporting information. Such additional pieces are not mandated by the regulation, although FDA might nevertheless incur other costs to integrate this electronic system into their overall information management system.

Table 6-29. FDA Web Portal Costs

Portal Costs	
Initial Development and Deployment	
Requirements - specifications	$30,000
Web and database design	$30,000
Web content (for general users, manufacturers, FDA)	$30,000
Web and database development	$100,000
Beta test	$30,000
Web/database revisions	$20,000
FDA clearance	$15,000
Initial outreach/training for manufacturers	$25,000
Initial deployment	$10,000
Initial population of database	$1,375,000
Unit Costs - One-Time	**$1,665,000**
Recurring Costs	
Hosting and maintenance	$40,000
Helpdesk	$5,000
Ongoing updating of database	$250,000
Unit Costs - Annual	**$295,000**

SECTION SEVEN
YEAR-BY-YEAR COST SAVINGS AND COSTS

Not all costs and cost savings that come as a result of the regulation will occur at once. In this section we present costs and cost savings on a year-by-year basis over the course of the first ten years after the regulation is published.

We begin by assuming that half of manufacturers, repackagers, and pharmacies will take steps to comply with the regulation in the first year after it is published and half will take steps to comply in the second year. This means that half of one-time costs discussed above and summarized in Table 7-1 occur in Year 1 and half occur in Year 2. To simplify the analysis, we use only the estimate of SPL conversion costs with its present value calculated at a 7 percent discount rate. Because manufacturers will have to continue to provide paper labels for two years after the rule is published, we assume that recurring annual costs and cost savings begin in Year 3.

Table 7-1. Basis for Cost and Cost Savings Estimates

	Cost Estimates		Cost Savings Estimates	
	Low	**High**	**Low**	**High**
Manufacturer and Repackagers				
One-time with SPL cost PV at 7%	$201,490,307	$339,706,957	$0	$0
Annual	$5,501,501	$20,528,238	$93,754,920	$216,541,480
Pharmacy				
One-time	$7,214,360	$18,717,291	$0	$0
Annual	$42,510,337	$75,709,241	$0	$0
Other Healthcare Providers				
One-time	$0	$0	$0	$0
Annual	$2,900,120	$10,352,964	$0	$0

The present value (*PV*) of annual costs and cost savings is calculated using the formula

$$PV = \frac{C}{(1+r)^t}, \text{ where}$$

C = the amount of annual costs or cost savings,

r =the discount rate (either 3 or 7 percent), and

t = the number of years after the regulation is published.

We use end of the year discounting, where costs are assumed to be incurred at the end of the year. The stream of costs and cost savings are presented in Table 7-2 by entity affected. The sum of the costs and cost savings across all entities are also presented.

Table 7-2. Costs and Cost Savings by Year ($1,000,000)

	Period of Payment										Total	Annualized Total
	1	2	3	4	5	6	7	8	9	10		
Manufacturer and Repackagers [a]												
Costs												
No Discount rate												
Low	$100.7	$100.7	$5.5	$5.5	$5.5	$5.5	$5.5	$5.5	$5.5	$5.5	$245.5	$24.6
High	$169.9	$169.9	$20.5	$20.5	$20.5	$20.5	$20.5	$20.5	$20.5	$20.5	$503.9	$50.4
3% Discount rate												
Low	$97.8	$95.0	$5.0	$4.9	$4.7	$4.6	$4.5	$4.3	$4.2	$4.1	$229.2	$26.9
High	$164.9	$160.1	$18.8	$18.2	$17.7	$17.2	$16.7	$16.2	$15.7	$15.3	$460.8	$54.0
7% Discount rate												
Low	$95.0	$88.0	$4.5	$4.2	$3.9	$3.7	$3.4	$3.2	$3.0	$2.8	$211.7	$30.1
High	$160.1	$148.4	$16.8	$15.7	$14.6	$13.7	$12.8	$11.9	$11.2	$10.4	$415.5	$59.2
Cost savings												
No Discount rate												
Low	$0.0	$0.0	$93.8	$93.8	$93.8	$93.8	$93.8	$93.8	$93.8	$93.8	$750.0	$75.0
High	$0.0	$0.0	$216.5	$216.5	$216.5	$216.5	$216.5	$216.5	$216.5	$216.5	$1,732.3	$173.2
3% Discount rate												
Low	$0.0	$0.0	$85.8	$83.3	$80.9	$78.5	$76.2	$74.0	$71.9	$69.8	$620.4	$72.7
High	$0.0	$0.0	$198.2	$192.4	$186.8	$181.4	$176.1	$170.9	$166.0	$161.1	$1,432.8	$168.0
7% Discount rate												
Low	$0.0	$0.0	$76.5	$71.5	$66.8	$62.5	$58.4	$54.6	$51.0	$47.7	$489.0	$69.6
High	$0.0	$0.0	$176.8	$165.2	$154.4	$144.3	$134.9	$126.0	$117.8	$110.1	$1,129.4	$160.8

Table 7-2. Costs and Cost Savings by Year ($1,000,000)

	Period of Payment										Total	Annualized Total
	1	2	3	4	5	6	7	8	9	10		
Pharmacy												
No Discount rate												
Low	$3.6	$3.6	$42.5	$42.5	$42.5	$42.5	$42.5	$42.5	$42.5	$42.5	$347.3	$34.7
High	$9.4	$9.4	$75.7	$75.7	$75.7	$75.7	$75.7	$75.7	$75.7	$75.7	$624.4	$62.4
3% Discount rate												
Low	$3.5	$3.4	$38.9	$37.8	$36.7	$35.6	$34.6	$33.6	$32.6	$31.6	$288.2	$33.8
High	$9.1	$8.8	$69.3	$67.3	$65.3	$63.4	$61.6	$59.8	$58.0	$56.3	$518.9	$60.8
7% Discount rate												
Low	$3.4	$3.2	$34.7	$32.4	$30.3	$28.3	$26.5	$24.7	$23.1	$21.6	$228.2	$32.5
High	$8.7	$8.2	$61.8	$57.8	$54.0	$50.4	$47.1	$44.1	$41.2	$38.5	$411.8	$58.6
Other Healthcare Providers												
No Discount rate												
Low	$0	$0	$2.9	$2.9	$2.9	$2.9	$2.9	$2.9	$2.9	$2.9	$23.2	$2.3
High	$0	$0	$10.4	$10.4	$10.4	$10.4	$10.4	$10.4	$10.4	$10.4	$82.8	$8.3
3% Discount rate												
Low	$0.0	$0.0	$2.7	$2.6	$2.5	$2.4	$2.4	$2.3	$2.2	$2.2	$19.2	$2.2
High	$0.0	$0.0	$9.5	$9.2	$8.9	$8.7	$8.4	$8.2	$7.9	$7.7	$68.5	$8.0
7% Discount rate												
Low	$0.0	$0.0	$2.4	$2.2	$2.1	$1.9	$1.8	$1.7	$1.6	$1.5	$15.1	$2.2
High	$0.0	$0.0	$8.5	$7.9	$7.4	$6.9	$6.4	$6.0	$5.6	$5.3	$54.0	$7.7
Total Costs												
No Discount rate												
Low	**$104.4**	**$104.4**	**$50.9**	**$50.9**	**$50.9**	**$50.9**	**$50.9**	**$50.9**	**$50.9**	**$50.9**	**$616.0**	**$61.6**
High	**$179.2**	**$179.2**	**$106.6**	**$106.6**	**$106.6**	**$106.6**	**$106.6**	**$106.6**	**$106.6**	**$106.6**	**$1,211.1**	**$121.1**
3% Discount rate												
Low	**$101.3**	**$98.4**	**$46.6**	**$45.2**	**$43.9**	**$42.6**	**$41.4**	**$40.2**	**$39.0**	**$37.9**	**$536.5**	**$62.9**
High	**$174.0**	**$168.9**	**$97.5**	**$94.7**	**$91.9**	**$89.3**	**$86.7**	**$84.1**	**$81.7**	**$79.3**	**$1,048.2**	**$122.9**

Table 7-2. Costs and Cost Savings by Year ($1,000,000)

	Period of Payment										Total	Annualized Total
	1	2	3	4	5	6	7	8	9	10		
7% Discount rate												
Low	**$98.3**	**$91.1**	**$41.6**	**$38.8**	**$36.3**	**$33.9**	**$31.7**	**$29.6**	**$27.7**	**$25.9**	**$455.0**	**$64.8**
High	**$168.8**	**$156.5**	**$87.0**	**$81.3**	**$76.0**	**$71.0**	**$66.4**	**$62.0**	**$58.0**	**$54.2**	**$881.3**	**$125.5**
Net Costs												
No Discount rate												
Low	**$104.4**	**$104.4**	**($42.8)**	**($42.8)**	**($42.8)**	**($42.8)**	**($42.8)**	**($42.8)**	**($42.8)**	**($42.8)**	**($238.4)**	**($23.8)**
High	**$179.2**	**$179.2**	**($110.0)**	**($110.0)**	**($110.0)**	**($110.0)**	**($110.0)**	**($110.0)**	**($110.0)**	**($110.0)**	**($700.4)**	**($70.0)**
3% Discount rate												
Low	**$101.3**	**$98.4**	**($39.2)**	**($38.1)**	**($37.0)**	**($35.9)**	**($34.8)**	**($33.8)**	**($32.8)**	**($31.9)**	**($185.1)**	**($21.7)**
High	**$174.0**	**$168.9**	**($100.6)**	**($97.7)**	**($94.8)**	**($92.1)**	**($89.4)**	**($86.8)**	**($84.3)**	**($81.8)**	**($558.6)**	**($65.5)**
7% Discount rate												
Low	**$98.3**	**$91.1**	**($35.0)**	**($32.7)**	**($30.5)**	**($28.5)**	**($26.7)**	**($24.9)**	**($23.3)**	**($21.8)**	**($132.3)**	**($18.8)**
High	**$168.8**	**$156.5**	**($89.8)**	**($83.9)**	**($78.4)**	**($73.3)**	**($68.5)**	**($64.0)**	**($59.8)**	**($55.9)**	**($416.9)**	**($59.4)**

[a] The SPL implementation cost included in the manufacturer and repackager costs is calculated at a 7 percent discount rate

Note: Numbers in parenthesis represent net cost savings

SECTION EIGHT

REGULATORY ALTERNATIVES

ERG developed costs for several alternatives involving shorter or longer implementation times for elements of the proposed regulatory change. Very short implementation times can create a number of additional costs to manufacturers and repackagers. For example, more of their existing stocks of paper copies of the professional PI will be discarded and they will encounter greater logistical challenges in generating new professional PI. Longer implementation times, on the other hand, might reduce losses of existing labeling stock and facilitate the incorporation of labeling changes into other voluntary relabeling activities.

As a baseline in estimating costs, ERG assumed that all professional PI will be required to be submitted to FDA in SPL format within six months after the final rule is published and that electronic PI will be required within two years. As alternatives, ERG considered scenarios where labels are not required to be submitted to FDA in SPL format for two years after the final rule is published, and where the switch from paper versions of the professional PI to electronic versions of the professional PI occurs either one year or three years after the final rule is published.

In order to estimate the cost impact of different compliance timelines for manufacturer submissions of professional PI in SPL, ERG spoke with providers of SPL conversion services. Provider A (2009) commented that in the case of a previous SPL regulation their SPL service had not faced capacity problems up to this point (although again this may have been due in part to low compliance). As noted previously in Section 6.1.8, in the event that the proposed SPL submission were required within six months, the data conversion service would respond by working overtime or shifting staff from projects with greater deadline flexibility. Increasing automation also will continue to increase capacity. However, no problems in capacity were foreseen with a two-year time frame. ERG presented the methodology for calculating costs for SPL conversion for a two-year time frame in Section 6.1.8 in Tables 6-19 and 6-20. Under the regulatory alternative of a two-year compliance time, total one-time costs for SPL conversion will range from $11.6 million to $14.6 million.

In order to estimate the cost impact of different compliance timelines for professional PI to be provided in exclusively electronic form, ERG spoke with industry experts to estimate additional costs that would accrue under shorter compliance timelines. ERG's conversations with printers who serve the pharmaceutical industry suggested that while a two to three year compliance timeline would be ideal (Printer D, 2009), printers judged that there would be no capacity constraints with even a six-month implementation period. They noted that they would be re-printing labels with a few additional lines of text (to direct healthcare professionals to electronic PI), which would not strain their printing capacity (Printer C, 2009). The printers say they only charge overtime for printing jobs with turnaround times of less than 24 hours. Printer C (2009) also said that most pharmaceutical printing is on a two-week to annual schedule, suggesting that the one-year timeline would in some cases not result in significant losses of inventory.

ERG assumes that inventory loss would be increased in the one year scenario and would vary with establishment size, as large brand manufacturers are on tighter production schedules and have more specialized personnel than small and medium brand manufacturers. We also judged that generic manufacturers' and repackagers' circumstance fall between these extremes. Accordingly we assume that under a one year compliance scenario small and medium brand manufacturers would lose 20 percent of their printed professional PI inventory, large brand manufacturers would lose 10 percent of their inventory, and generic manufacturers and repackagers would lose 17 percent of their inventory (Expert A,

2009). Under a two or three year compliance timeline, we assume that there would be no loss of printed professional PI inventory beyond the irreducible minimum used in the baseline analysis.

ERG also assumed that requiring electronic versions of the professional PI within one year after the final rule is published would increase label change costs. Although no industry representatives with whom we spoke foresaw capacity constraints resulting from a one year compliance timeline, we increase label change costs by 10 percent to account for any unforeseen difficulties in coordinating these changes industry-wide.

Under these assumptions and the same high and low estimates used elsewhere in the cost analysis, ERG produced a range of estimates for requiring electronic PIs within one, two and three years and requiring SPL submissions for unapproved and repackaged drugs within six months and two years of when the final rule is published (see Table 8-2). With our assumptions that inventory loss and label change costs would only be increased if compliance were required within one year, costs under the three year scenario are identical to costs under the baseline two-year scenario presented above.

Annualizing costs at a 3 percent discount rate and assuming labels must be provided in electronic form in one year, total costs with six-month SPL implementation range from $80.3 million to $159.5 million, and total costs with two-year SPL implementation range from $80.1 million to $159.3 million. Annualizing costs at a 7 percent discount rate and assuming labels must be provided in electronic form in one year, total costs with six-month SPL implementation range from $86.5 million to $170.4 million, and total costs with two-year SPL implementation range from $86.2 million to $170.1 million.

As in the case of annual costs, annualized costs under the two and three year compliance scenarios are identical. Annualizing costs at a 3 percent discount rate and assuming labels must be provided in electronic form in either two or three years, total costs with six-month SPL implementation range from $75.5 million to $148.8 million, and total costs with two-year SPL implementation range from $75.3 million to $148.5 million. Annualizing costs at a 7 percent discount rate and assuming labels must be provided in electronic form in either two or three years, total costs with six-month SPL implementation range from $80.8 million to $157.8 million, and total costs with two-year SPL implementation range from $80.6 million to $157.5 million.

Table 8-1. SPL Conversion Costs Under Two Year and Six Month Compliance Scenarios

Costs	6 Month Implementation Total Cost (Present Value)				2-Years Implementation Total Cost	
	3%		7%			
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate
Initial conversion	$9,024,000	$11,280,000	$8,352,000	$10,440,000	$8,000,000	$10,000,000
QA review of converted file	$3,451,978	$4,314,972	$3,194,916	$3,993,645	$3,060,264	$3,825,330
Cost to validate new SPL submission process	$621,356	$897,514	$575,085	$830,678	$550,848	$795,669
Total one-time cost	**$13,097,334**	**$16,492,486**	**$12,122,000**	**$15,264,323**	**$11,611,112**	**$14,620,999**

Annualized Costs	6 Month Implementation Annualized				2-Years Implementation Annualized			
	3%		7%		3%		7%	
	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate	Low Estimate	High Estimate
Initial conversion	$1,057,888	$1,322,360	$1,284,815	$1,606,018	$937,844	$1,172,305	$1,139,020	$1,423,775
QA review of converted file	$404,677	$505,846	$491,484	$614,355	$358,756	$448,445	$435,713	$544,641
Cost to validate new SPL submission process	$72,842	$105,216	$88,467	$127,786	$64,576	$93,277	$78,428	$113,285
Total one-time cost	**$1,535,407**	**$1,933,423**	**$1,864,766**	**$2,348,159**	**$1,361,176**	**$1,714,027**	**$1,653,161**	**$2,081,701**

Table 8-2. Annualized Cost Comparison of Regulation and Regulatory Alternatives

Cost Savings	**Low Estimate**		**High Estimate**	
Manufacturers	$20,988,420		$52,628,980	
Repackagers	$72,766,500		$163,912,500	
Total Cost Savings	**$93,754,920**		**$216,541,480**	
Costs	**3% Discount Rate**		**7% Discount Rate**	
	Low Estimate	**High Estimate**	**Low Estimate**	**High Estimate**
1 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$9,732,785	$23,108,739	$11,373,049	$26,411,078
Repackagers	$22,750,366	$46,168,345	$26,780,465	$52,884,669
Total Costs (without SPL costs)	$78,739,350	$157,533,527	$84,591,132	$168,022,873
Total Costs (with 6 month SPL implementation)	**$80,274,757**	**$159,466,949**	**$86,455,898**	**$170,371,032**
Total Costs (with 2 years SPL implementation)	**$80,100,527**	**$159,247,554**	**$86,244,293**	**$170,104,574**
2 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$8,531,861	$20,173,157	$9,954,736	$22,994,603
Repackagers	$19,169,383	$38,389,655	$22,508,552	$43,726,967
Total Costs (without SPL costs)	$73,957,443	$146,819,255	$78,900,907	$155,448,696
Total Costs (with 6 month SPL implementation)	**$75,492,850**	**$148,752,677**	**$80,765,672**	**$157,796,855**
Total Costs (with 2 years SPL implementation)	**$75,318,619**	**$148,533,282**	**$80,554,068**	**$157,530,397**
3 Year Implementation				
Users of PI (pharmacists, physicians, others)	$46,256,200	$88,256,442	$46,437,619	$88,727,126
Manufacturers	$8,531,861	$20,173,157	$9,954,736	$22,994,603
Repackagers	$19,169,383	$38,389,655	$22,508,552	$43,726,967
Total Costs (without SPL costs)	$73,957,443	$146,819,255	$78,900,907	$155,448,696
Total Costs (with 6 month SPL implementation)	**$75,492,850**	**$148,752,677**	**$80,765,672**	**$157,796,855**
Total Costs (with 2 years SPL implementation)	**$75,318,619**	**$148,533,282**	**$80,554,068**	**$157,530,397**

SECTION NINE

PUBLIC HEALTH BENEFITS OF THE PROPOSED PAPERLESS LABELING RULE

9.1 BENEFITS OF THE PROPOSED REGULATION

The proposed regulation would provide pharmacists and other healthcare providers with a single source for up-to-date information on product safety through electronic means. This section considers the potential impacts of the rule on public health.

The argument that a shift to electronic versions of the professional PI would improve public health is outlined by the American Society of Health-System Pharmacists (ASHP, 2007):

> ASHP firmly believes that electronic distribution and access of the prescribing information would improve public health by expanding access to such information. Electronic information cannot be thrown away, can be accessed via the Internet at any time and from many locations, and if updated on a regular basis, is more timely and accurate than traditional paper sources. Furthermore, research has shown that a large number of prescribing errors are attributable to the prescribers' lack of knowledge about a drug. Prescribers with access to electronic prescription information would potentially have current drug information more readily available and accessible, which might lead to fewer prescribing errors. Prescribing habits would be improved, contributing to the overall improvement of public health.

Electronic PI improves the timeliness of the PI because the PI need not accompany the physical package through the pharmaceutical supply chain. Most pharmaceutical products have a product life of two years from manufacturer and some products are not actually used until very late in that two-year period. During this time new safety information about the drug or a new warning for a range of pharmaceutical products in general might be developed. Despite FDA's or the manufacturer's efforts, health care professionals would not necessarily be aware of the new information and might rely on the outdated PI that accompanies the drug product.

Currently healthcare providers become aware of important new drug safety information through a variety of means such as colleagues, medical journals, and newsletters. FDA or pharmaceutical manufacturers can use "Dear Doctor" or "Dear Health Care Professional" Letters to disseminate relatively urgent pharmaceutical or other medical problem data on short notice. For example, Mazor (2005) found that 123 drugs had changes to the warning section of their label in 2000 and 2001, with Dear Doctor Letters sent to address 26 percent of these changes.

However, such letters are not entirely effective communication. According to the Mazor study, physicians found that about one quarter to one third of the "Dear Doctor" letters to be lacking in clarity, readability, and other important characteristics. Further, because of the general volume of product safety and health care information crossing a physician's or pharmacist's desk, it is reasonable to think that no type of notification is certain to be received, read, and incorporated into the provider's understanding and practice.

For less urgent information, neither FDA nor pharmaceutical manufacturers would be likely to use a "Dear Doctor" Letter. Pharmacists can sign up to receive daily or weekly email updates from FDA regarding drug changes. A hyperlink imbedded in the alert allows the receiver to access the website for the drug in question. Under the current system, the updated version of the professional PI is not always

immediately posted on FDA's website, but the pharmacist can find it on the manufacturer's website (Pharmacist A et al., 2009). Pharmacists who do not receive these alerts from FDA might remain unaware of the information modified from that in the old printed PI. With an electronic database of professional PI, some of these problems would be eliminated and healthcare providers could be certain that the drug information they access via FDA's website is the most up to date.

If pharmacists and physicians also referred to an electronic PI more frequently than to the paper version, a public health benefit should result. For pharmacists the notion that electronic PI will be accessed more frequently than that in paper PI was supported by trials conducted by the Pharmaceutical Research and Manufacturers of America's (PhRMA) paperless PI task force. While based on self-report and not measurements of actual behavior, the PhRMA task force found that 69 percent of pharmacists in the trial using Thomsen's "PDR on Demand" device said that they would "definitely" or "probably" use it more frequently than they use paper PI (Ukens, 2005). PDA-based Epocrates database of drug information is similarly thought to save time, improve drug-related decision making, and reduce the rate of preventable adverse drug events (Rothschild et al., 2002).

9.2 LIMITING FACTORS TO ACCRUAL OF PUBLIC HEALTH BENEFITS

Despite these potential public health benefits, it is worth noting that many drug-related errors and adverse events stem from factors that would not be affected by the change. For example, Flynn et al.'s (2003) study of pharmacy errors found that the most common type concerned problems with the label and instructions affixed to the medication given to the patient and stemmed from errors in the computer order entry process used to create the label. Drug-related errors have also been found to be associated with increased pharmacist workload (Bond & Raehl, 2001; Malone et al., 2007; Szeinbach et al., 2007), low job satisfaction (Bond & Raehl, 2001), staffing (Bond & Raehl, 2001), training, (Bond & Raehl, 2001), professional organization membership (Bond & Raehl, 2001), pharmacy design (Szeinbach et al., 2007), and cognitive errors (Szeinbach et al., 2007).

SECTION TEN

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ANDA	Abbreviated New Drug Application
APhA	American Pharmacists Association
APS	Automatic Picking System
ASHP	American Society of Health-System Pharmacists
BLA	Biologic License Application
BLS	Bureau of Labor Statistics
COGME	Council on Graduate Medical Education
e-DRLS	Electronic Drug Registration and Listing Systems (e-DRLS)
EPA	Environmental Protection Agency
ERG	Eastern Research Group, Inc.
FDA	Food and Drug Administration
GPhA	Generic Pharmaceutical Association
HDMA	Healthcare Distribution Management Association
IV	Intravenous
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
MGMA	Medical Group Management Association
NABP	National Association of Boards of Pharmacy
NACDS	National Association of Chain Drug Stores
NDA	New Drug Application
NDC	National Drug Code
NLM	National Library of Medicine
PDA	Personal Digital Assistant
PDR	Physicians Desk Reference
PhRMA	The Pharmaceutical Research and Manufacturers of America
PI	Prescribing Information
PPI	Patient Package Insert
SKU	Stock Keeping Unit
SPL	Structured Product Language
USP	U.S. Pharmacopoeia
XML	Extensible Markup Language

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