DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Use of Symbols in Labeling

Docket No. (FDA-2013-N-0125)

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

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I. Introduction and Summary

A. Introduction

FDA has examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that the final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because manufacturers can choose whether to adopt the requirements proposed under this rule, and are only expected to do so when they expect a net benefit, the agency certifies that the final rule is not expected to impose any new substantial burdens on small entities, and thus is not expected to impose a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may

result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

B. Summary

The final rule would provide medical device manufacturers with the option to use symbols established in a standard developed by a standards development organization (SDO) in medical device labeling without adjacent explanatory text as long as: (a) the standard is recognized by FDA under its authority under section 514(c) of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 360d(c)) and the symbol is used according to the specifications for use of the symbol set forth in FDA's section 514(c) recognition, or alternatively, (b) if the symbol is not included in a standard recognized by FDA under section 514(c) of the FD&C Act or the symbol is in a standard recognized by FDA but is not used according to the specification for use of the symbol set out in the FDA section 514(c) recognition, the device manufacturer otherwise determines that the symbol is likely to be read and understood by the ordinary individual under customary conditions of purchase and use in compliance with section 502(c) of the Act and uses the symbol according to the specifications for use of the symbol set forth in the SDO-developed standard; and, in either case, the symbol is explained in a paper or electronic symbols glossary that is included in the labeling for the medical device and the labeling

on or within the package containing the device must bear a prominent and conspicuous statement identifying the location of the symbols glossary that is written in English or, in the case of articles distributed solely in Puerto Rico or in a Territory where the predominant language is one other than English, the predominant language may be used. This option would allow manufacturers to substitute labels containing only written statements (text-only labels) with a label containing stand-alone symbols, provided that such symbols are explained in a written or electronic symbols glossary that is included in the labeling for the medical device. The final rule also revises prescription device labeling regulations to allow the use of the symbol statement "Rx only" or "℞ only" in the labeling for prescription devices.

Medical device manufacturers would only choose to use stand-alone symbols, as allowed by the final rule, if they expect a positive net benefit (estimated benefits minus estimated costs). Hence, the final rule is expected to provide a non-negative net benefit to each adopting manufacturer that opts to use stand-alone symbols. Choosing to use stand-alone symbols under the final rule would potentially reduce the costs associated with designing and re-designing the labels on medical devices that are currently marketed in the U.S. and the European Union (EU). The estimated annual benefits range from $7.9 million to $25.5 million at a 3 percent discount rate, and $7.7 million to $25.0 million at a 7 percent discount rate. Those that opt to use stand-alone symbols under the rule would incur one-time administrative costs (such as redesigning the label and creating a symbols glossary that is included in the labeling for the device), which we estimate to range from $3.5 million to $9.8 million for all manufacturers. Annualized over 20 years, net benefits

range from $7.6 million to $24.9 million at a 3 percent discount rate, and from $7.4 million to $24.1 million at a 7 percent discount rate. The costs and benefits accrue to the same entities, however, so any firm making the change to stand-alone symbols would, on net, reduce costs.

II. Final Regulatory Impact Analysis

A. Background

Medical devices are sold worldwide. To participate in most international markets, medical device manufacturers must communicate certain information to end users, such as the manufacturer's identity, the device's intended use, and directions for use. Most countries require this information to appear in their national language. However, some countries, such as the members of EU, also allow this information to appear as standardized international symbols, such as those documented in ISO 15223 and EN 980:2008.

Using standardized international symbols (henceforth referred to as symbols for short) may substantially benefit both medical device manufacturers and end users. Medical device manufacturers that export to the EU can use symbols to reduce the costs associated with designing and re-designing labels for both the U.S. and EU. For instance, some medical device labels can communicate the same information using text-only labels or labels with stand-alone symbols. In this case, manufacturers who export medical devices can use the same set of stand-alone symbols, per uniquely labeled medical device, on labeling in every nation recognizing these symbols., This practice is cheaper

than using text-only labels for the U.S. and Puerto Rico and stand-alone symbols on labeling for the rest of the World, which would require manufacturers to work with two types of symbols (stand-alone symbols and symbols with adjacent explanatory text) for their labeling of devices.

Using stand-alone symbols could also benefit end users. Stand-alone symbols use less physical space than the text for which they substitute. Manufacturers could use the extra space to make their label more understandable. For instance, they could include more detailed instructions, increase the size of the remaining text, or space out the written statements to make the label easier to read.

B. Benefits

Adopting the rule would potentially reduce the costs associated with designing and re-designing the labels on medical devices that are currently sold in the U.S. and EU. The principal beneficiaries in the U.S. are exporters: U.S. manufacturers who export medical devices to the EU. The rule would allow an exporter to use the same set of stand-alone symbols on a device labeling in the U.S. and EU, thus saving the exporter the resources associated with designing and re-designing the labeling to include symbols with adjacent explanatory text to use in the U.S.

FDA assumes that the labeling of each uniquely labeled medical device can communicate the same information using stand-alone symbols or symbols with adjacent explanatory text. FDA further assumes that exporters currently use text-only labelings in

the U.S. market, and labelings with stand-alone symbols in the EU. Exporters probably use labels with stand-alone symbols in the EU because it is cheaper to a design labeling with a common set of stand-alone symbols versus creating a labeling with no symbols for each EU nation with a different national language. The same rationale suggests that exporters would probably opt to use a single set of stand-alone symbols in a device labeling for markets in the U.S. and EU, rather than continue to create and mix no symbols, stand-alone symbols, and symbols with adjacent explanatory text on a labeling for various markets. As a result, exporters would avoid the costs associated with designing and re-designing multiple formats when symbols are used in labeling for medical devices sold in both the U.S. and EU.

The final rule would provide exporters with the option to use a single format for stand-alone symbols in the labeling of devices marketed in the U.S. and EU. This option allows exporters to avoid the costs associated with using no symbols or creating a separate format for symbols with adjacent explanatory text on a labeling for devices marketed in the U.S., particularly, for new medical device products. Estimating these costs requires data that projects the number of new medical devices that manufacturers are expected to sell in the future. Because these data are unavailable, we cannot quantify this particular benefit.

Medical device manufacturers regularly revise and re-design their labels in response to changes in markets, regulations, and technology. The final rule would allow exporters to avoid the costs associated with re-designing separate U.S. and EU labels

each time they make a change using a symbol. Total label re-design costs are roughly equal to re-design costs multiplied by the number of labels [=(the average cost associated with re-designing medical device labels) x (the number of unique medical device labels used in the U.S. and EU)]. Data on the latter is unavailable. To calculate this value, we assume that each uniquely labeled medical device contains a labeling that can communicate the same information using either a stand-alone symbols or symbols with adjacent explanatory text.

FDA assumes that the number of uniquely labeled medical devices sold in the U.S. and EU is approximately equal to the total estimated number of uniquely labeled medical devices that U.S. companies produce multiplied by the percentage sold in the U.S. and EU. Table 1 presents these data. We assume that the percentage of uniquely labeled medical devices sold in the U.S. and EU is roughly equal to the ratio of EU sales to total U.S. sales (= value of total medical device sales in the EU in 2013 / value of total U.S. medical device sales in 2013). U.S. International Trade Commission reports that the total value of U.S. medical device sales in the EU equaled $20 billion in 2013 (Ref. E1), while the 2013 Annual Survey of Manufacturers reports that the total value of medical device sales equaled $157 billion in 2013 dollars (Ref. E2). U.S. International Trade Commission and the 2013 Annual Survey of Manufacturers classify industries using the North American Industry Classification System (NAICS). To estimate the above values, we used the NAICS codes associated with those medical device industries participating in international trade: 325413, 334510, 334516, 334517, 339112, 339113. 339114, and 339115.

TABLE 1—ESTIMATED NUMBER OF UNIQUE LABELS FOR MEDICAL DEVICES SOLD IN THE US AND EU

	Number of Establishments
Company Size	
Medium to Large	154
Small	1,235
Very Small	5,742
	Average Number of Unique Labels for Medical Devices Sold in the US and EU
Company Type	
Medium to Large	205.4
Small	39.85
Very Small	13.7
Total U.S. Medical Device Sales in 2013 (in $1,000s)	157,362,931
Total Value of Medical Devices Sales in EU in 2013 (in $1,000s)	19,791,643
Value Total Sales in EU to Total Medical Device Sales in 2013	0.126
Estimated Number Unique Labels used in US and EU	20,062

Notes—Rounding may produce slight variations to the above estimates. The 2012 Economic Census reports the total number of establishments. The 2013 Annual Survey of Manufacturers reports the total value of medical device sales in 2013. To calculate this number, we used NAICS codes 325413, 334510, 334516, 334517, 339112, 339113, 339114, and 339115. Average EU sales were calculated using data from 2013. Sales are in ($1,000s)

FDA assumes that the total estimated number of uniquely labeled medical devices produced by U.S. companies approximately equals the number of U.S. medical device manufacturers multiplied by the average number of uniquely labeled medical devices they produce. However, larger establishments probably produce more uniquely labeled medical devices than smaller establishments, on average. Hence, to compute the total estimated number produced, we performed the following steps: first, we separated companies by size; second, we estimated the number of companies within each size category; third, we estimated the average number of uniquely labeled medical devices produced within each company size category; fourth, we took the product of these estimates within each size category; and finally, we summed the products.

The Small Business Administration classifies most device manufacturing firms as small if they have fewer than 500 employees (Ref. E3). We further categorize companies

into the following size categories: very small sized establishments that employ fewer than 100 employees; small sized establishments that employ fewer than 500 employees but more than 99 employees; and finally, medium-to-large sized establishments that employ 500 or more employees. We use the 2012 Economic Census to estimate the number of medical device establishments in each size category (Ref. E4). We do not use the 2013 Annual Survey of Manufacturers to estimate this value because it does not report how many companies employ fewer than 500 employees.

To estimate the average number of uniquely labeled medical devices by establishment size, we randomly sampled approximately 157 very smallsized manufacturers, 20 small sized manufacturers and 10 medium to large sized manufacturers. The Technical Appendix discusses the data source and its construction in detail. The results indicate that very small, small, and medium to large establishments sell approximately 13.7, 39.85, and 205.4 uniquely labeled medical devices, on average, respectively. Given these data, we estimate that U.S. medical device companies use approximately 20,062 unique medical device labelings (= 0.126 ratio of EU sales to total U.S. sales * [13.7 labels per very small establishment * 5,742 very small establishments + 39.85 labels per small establishment * 1,235 small establishments + 205.4 labels per medium to large establishment * 154 medium to large establishments]) in the U.S. and EU (Table 1). The above estimated value might not correspond to the value calculated in parenthesis due to rounding.

We estimate the average cost of re-designing a unique medical device label to incorporate a new or changed symbol, or set of symbols, using a model developed by a contractor, RTI International (Ref. E5). The model does not cover every medical device industry studied above. However, it does examine a relatively similar industry: retail medical device manufacturers (NAICS codes 322121, 325412, 325413, 325620, 326299, 335211, 339112, 339113, 339114, and 339994). We capture the average cost to re-design a medical device label using the costs associated with re-designing retail medical devices. The model proxies the latter cost using the average re-design costs per universal product. We recognize that re-designing costs are not the same across these two industries; however, these are the best data available to study this topic.

Changing labels commonly requires the following resources: labor, materials, inventory, market testing, analytical testing, and recordkeeping. The costs associated with using these resources vary with compliance time. More compliance time reduces costs as it enables manufacturers to coordinate more labeling activities. Because companies want to minimize costs, we assume that every adopting company would start using stand-alone symbols once it is possible to maximize coordinating resources. Once companies start using stand-alone symbols, we assume every proceeding revision occurs at the average re-design rate. The RTI model indicates that the average label re-design rate among medical device manufacturers is approximately once every 3.25 years, and that the re-designs in question—converting written statements to stand-alone symbols, and making revisions to the glossary—are minor changes that only requires some labor and recordkeeping resources (Ref. E5). Medical devices enter the market at various times,

and thus not all device labels are revised at the same time. Because revisions occur approximately every 3.25 years, on average, we assume that roughly one third of the current stock of medical devices is revised every year. This assumption suggests that approximately 6,173 (= 20,062/3.25) labels are revised every year.

Table 2 reports the average initial re-design costs per label and the average proceeding re-design costs per label On average, the initial costs associated with labor range from $176 to $490, while recordkeeping costs range from $38 to $63. The average proceeding re-design costs associated with using labor range from $1,297 to $4,295, while recordkeeping costs range from $52 to $91. Subsequent relabeling costs are greater than initial relabeling costs because manufacturers are expected to introduce the labeling changes associated with this rule when they are planning their next labeling change (i.e., when they can coordinate/leverage existing resources). In contrast, not every manufacturer is expected to be able to make future labeling changes when it is convenient to do so, resulting in a greater average cost.

TABLE 2—ESTIMATED LABELING RE-DESIGNING COSTS

Cost Factor (Coordinated)	Low	Midpoint	High
Labor……	175.83	339.09	489.80
Recordkeeping……	37.68	50.24	62.80
Cost Factor (Coordinated & Uncoordinated)	**Low**	**Midpoint**	**High**
Labor……	1297.11	2476.54	4295.16
Recordkeeping……	51.69	78.27	90.83
Total Per Label Costs	**Low**	**Midpoint**	**High**
Initial Coordinated Labeling Re-designs……..	213.50	389.33	552.60
Future Labeling Re-designs……..	1,348.80	2,554.81	4,385.99

Note: Coordinated labeling changes occur when the manufacturer is already scheduled to change a label.

Table 3 reports the estimated total quantified benefits. Using a 20 year time horizon, the total present discounted value of benefits range from $117.1 million to $379.8 million at a 3 percent discount rate, and from $81.7 million to $264.7 million at a 7 percent discount rate. Annualized over 20 years, total benefits range from $7.9 million to $25.5 million at a 3 percent discount rate, and from $7.7 million to $25.0 million at a 7 percent discount rate.

TABLE 3—ESTIMATED LABELING RE-DESIGNING COSTS			
Labeling Re-design Savings	Low	Midpoint	High
Total Labeling Re-design Costs Avoided			
3 Percent	117,067,890	221,652,144	379,829,123
7 Percent	81,657,545	154,583,528	264,714,494
Annualized Labeling Re-design Costs Avoided			
3 Percent	7,868,801	14,898,506	25,530,483
7 Percent	7,707,895	14,591,591	24,987,176

The above analysis captures the upper bound estimate for benefits because it assumes that every labeling may be able to use the same single format for stand-alone symbols on the device labeling. However, it is possible that some labels might not be able to use the same set of stand-along symbols, implying that our estimate might overstate benefits.

C. Costs

Firms will only voluntarily choose to use stand-alone symbols in labeling, as allowed by the final rule, if they expect to save labeling costs or experience other benefits, on net. However, companies would incur some potential costs in order to use stand-alone symbols, such as one-time administrative and outreach costs. Furthermore,

some studies indicate that end users may be more likely to misinterpret stand-alone symbols than written statements. These studies suggest that using stand-alone symbols, without an accompanying symbols glossary, may cause more end users to use medical devices incorrectly, resulting in potentially more medical errors and thus more adverse events, all else the same (Ref. E6). However, including a symbols glossary should ameliorate this problem.

1. Administrative Costs

Choosing to use stand-alone symbols, as allowed by the final rule, would require one-time administrative costs (i.e. labor costs associated with administrative activities, such as determining the best way to implement stand-alone symbols and revise the associated symbols glossary). We use the labeling cost model to estimate this cost. Table 4 reports the average administrative costs associated with choosing to use stand-alone symbols, as allowed by the final rule. The model estimates the average administrative costs per Universal Product Code to range from $176 to $490. Total one-time administrative costs range from $3.5 million to $9.9 million.

TABLE 4—ADMINISTRATIVE COSTS

	Low	Midpoint	High
Administrative Costs per UPC……	175.83	339.09	489.8
Estimated Total Medical Device UPC……	20,062	20,062	20,062
Total One-Time Administrative Costs……	3,527,501	6,802,824	9,826,368

2. Outreach

We estimate incremental outreach costs to be approximately zero. Under the final rule, one requirement of using stand-alone symbols is that they are explained in a paper or electronic symbols glossary that is included in the labeling for the device.. In addition to the administrative costs estimated above, revising the symbols glossary requires manufacturers to physically change the wording during the first relabeling. As stated above, we assume manufacturers would start using stand-alone symbols once it is possible to coordinate resources; e.g. when they are already in the process of physically changing the wording of their labeling. Because manufacturers are already making changes to their labeling, the labeling cost model estimates any additional costs to changing the glossary to approximately equal zero. To the extent that any other costs occur, however, we assume it would be included in our estimated administrative costs.

3. Adverse Events

The available empirical evidence suggests that end users would be more likely to misinterpret non-standardized, stand-alone symbols than written statements, resulting in more medical errors that translate to adverse events. For instance, Liu et al. (Ref. E6) estimated the percentage of German nurses and doctors that could comprehend the stand-alone symbols recognized in the EU. Their results indicate that most nurses and doctors misunderstood non-standard, stand-alone symbols intended to communicate instructions aimed at preventing adverse events. For example, roughly 75 percent of nurses and doctors misunderstood the stand-alone symbol intended to convey “do not re-use”.

Estimating the potential costs associated with misinterpreting stand-alone symbols requires the following data: the rate with which end users misinterpret stand-alone symbols, the extent to which misinterpreting stand-alone symbols translates to an adverse event, the average severity of adverse events associated with misinterpreting stand-alone symbols, and the end user's willingness-to-pay to avoid such an adverse event. These data are unavailable, however, and thus this cost cannot be quantified. Nevertheless, the expected costs are probably quite small. The most severe, and thus costly, adverse events are expected to occur under the riskiest medical devices. However, we expect that the riskiest medical devices are only operated by medical professionals. Even if these professionals are not aware of the devices' potential hazards, either through training and/or consulting the device's instruction manual, requiring a symbols glossary will help these professionals be able to read and understand stand-alone symbols used in device labeling. Furthermore, the rule proposes manufacturers use standard, stand-alone symbols that are already well-established and recognizable.

4. Total Estimated Costs

One-time administrative costs are the only expected costs associated with using stand-alone symbols, as allowed by the final rule. Table 5 reports the total estimated costs. Annualized over 20 years, total estimated costs range from $0.24 million to $0.66 million at a 3 percent discount rate, and from $0.33 million to $0.93 million at a 7 percent discount rate.

TABLE 5—TOTAL ESTIMATED COSTS

Cost Factor	Low	Midpoint	High
Total One-Time Administrative Costs	3,527,426	6,802,892	9,826,400
Annualized Cost			
3 Percent	237,098	457,261	660,488
7 Percent	332,964	642,145	927,543

D. Summary of Costs and Benefits

Table 6 presents the estimated quantified annualized costs, benefits and resulting net benefits associated with adopting the final rule. Annualized over 20 years, net benefits range from $7.6 million to $24.9 million at a 3 percent discount rate, and from $7.4 million to $24.1 million at a 7 percent discount rate.

TABLE 6—ESTIMATED ANNUALIZED NET BENEFITS

Description	Low	Midpoint	High
Annualized Benefits			
3 Percent	7,868,801	14,898,506	25,530,483
7 Percent	7,707,895	14,591,591	24,987,176
Annualized Costs			
3 Percent	237,098	457,261	660,488
7 Percent	332,964	642,145	927,543
Annualized Net Benefits			
3 Percent	7,631,703	14,441,244	24,869,995
7 Percent	7,374,931	13,949,447	24,059,633

E. Uncertainty Analysis and Sensitivity Analysis

The final rule would provide medical device manufacturers with the option to use symbols established in a standard developed by a standards development organization (SDO) in medical device labeling without adjacent explanatory text as long as: (a) the standard is recognized by FDA under its authority under section 514(c) of the Federal

Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 360d(c)) and the symbol is used according to the specifications for use of the symbol set forth in FDA's section 514(c) recognition, or alternatively, (b) if the symbol is not included in a standard recognized by FDA under section 514(c) of the FD&C Act or the symbol is in a standard recognized by FDA but is not used according to the specification for use of the symbol set out in the FDA section 514(c) recognition, the device manufacturer otherwise determines that the symbol is likely to be read and understood by the ordinary individual under customary conditions of purchase and use in compliance with section 502(c) of the Act and uses the symbol according to the specifications for use of the symbol set forth in the SDO-developed standard; and, in either case, the symbol is explained in a paper or electronic symbols glossary that is included in the labeling for the medical device and the labeling on or within the package containing the device bears a prominent and conspicuous statement identifying the location of the symbols glossary that is written in English or, in the case of articles distributed solely in Puerto Rico or in a Territory where the predominate language is one other than English, the predominant language may be used. This option allows manufacturers to substitute labels containing text-only labels with labels with stand-alone symbols.

1. Label Revision Rates

The total estimated net benefits associated with using stand-alone symbols are highly sensitive to labeling costs, which are contingent upon the rate at which medical device manufacturers revise their labels; the higher the rate, the greater are the cost savings from reducing the number of labels per product. The RTI model indicates that the

mean revision rate is roughly once every 3 years. However, this revision rate may overstate the rule's total estimated benefits because the rate applies to the retail medical device industry, who we expect revises their labels more regularly than the non-retail medical device industry.

One alternative to using the mean revision rate is the mode: the most frequent revision rate. According to the labeling cost model, the most common revision rate is once every 5 years (Ref. E3). During the 5th year, retail medical device companies revise approximately 50 percent of their labels. This rate is substantially greater than every other revision rate (e.g., during the second most common revision rate year, medical device companies only revise approximately 20 of their labels). If revisions occur every 5 years, on average, roughly one fifth of the current stock of medical devices would be revised every year. As a result, we expect medical device companies to now revise approximately 4,012 (= 20,062/5) labels every year.

Table 7 presents the total estimated benefits associated with an average revision rate of 5 years. The results indicate that extending the revision rate by approximately two more years corresponds to a moderate reduction in total expected benefits. The reduction is attributed to medical device companies using the extra time to coordinate more productive resources, resulting in substantially lower resource costs. As a result, total estimated benefits now range from $76.1 million to $246.9 million at a 3 percent discount rate, and from $53.1 million to $172.0 million at a 7 percent discount rate. Annualized over 20 years, total estimated benefits range from $5.0 million to $16.6 million.

TABLE 7—ESTIMATED LABELING RE-DESIGNING COSTS

Revision Rate = 5 years			
Labeling Re-design Savings	Low	Midpoint	High
Total Labeling Re-design Costs Avoided			
3 Percent	76,085,594	144,057,736	246,861,241
7 Percent	53,071,452	100,468,024	172,045,124
Annualized Labeling Re-design Costs Avoided			
3 Percent	5,114,147	9,682,943	16,592,953
7 Percent	5,009,570	9,483,471	16,239,843
Revision Rate = 1.5 years			
Labeling Re-design Savings	Low	Midpoint	High
Total Labeling Re-design Costs Avoided			
3 Percent	253,650,255	480,252,297	822,973,355
7 Percent	176,926,886	334,935,151	573,555,217
Annualized Labeling Re-design Costs Avoided			
3 Percent	17,049,281	32,280,498	55,316,736
7 Percent	16,700,646	31,615,509	54,139,555

Table 8 presents the total estimated net benefits associated with an average revision rate of 5 years. Extending the revision rate does not change the total costs associated with using stand-alone symbols, and thus increasing the revision rate time period only changes the total estimated net benefits via changing total estimated benefits. Annualized over 20 years, net benefits range from $4.9 million to $15.9 million at a 3 percent discount rate, and from $4.7 million to $15.3 million at a 7 percent discount rate.

TABLE 8—ESTIMATED ANNUALIZED NET BENEFITS

Description	Low	Midpoint	High
Revision Rate = 5 years			
Annualized Benefits			
3 Percent	5,114,147	9,682,943	16,592,953
7 Percent	5,009,570	9,483,471	16,239,843
Annualized Costs			
3 Percent	237,098	457,261	660,488
7 Percent	332,964	642,145	927,543
Annualized Net Benefits			
3 Percent	4,877,049	9,225,681	15,932,465
7 Percent	4,676,606	8,841,326	15,312,300
Revision Rate = 1.5 years			
Annualized Benefits			
3 Percent	17,049,281	32,280,498	55,316,736
7 Percent	16,700,646	31,615,509	54,139,555
Annualized Costs			
3 Percent	237,098	457,261	660,488
7 Percent	332,964	642,145	927,543
Annualized Net Benefits			
3 Percent	16,812,183	31,823,237	54,656,248
7 Percent	16,367,682	30,973,364	53,212,012

Changing economic conditions (e.g., an increase in competition or changes in regulation) could encourage companies to revise their labels more rapidly than originally planned. According to the labeling cost model, the quickest revision rate occurs once every 1.5 years, which is when approximately 10 percent of retail medical device companies revise their labels. If revisions occur once every 1.5 years, on average, then we assume that roughly two-thirds of the current stock of medical device labels would be revised every year. As a result, we expect medical device companies to now revise approximately 13,375 (= 20,062/1.5) labels every year.

Table 7 presents the total estimated benefits associated with an average revision rate of 1.5 years. The results indicate that reducing the revision rate approximately two

years corresponds to a substantial increase in total expected benefits. The increase corresponds to the substantial amount of uncoordinated resources that companies can avoid via switching to using stand-alone symbols. As a result, total estimated benefits now range from $253.7 million to $823.0 million at a 3 percent discount rate, and from $176.9 million to $573.6 million at a 7 percent discount rate. Annualized over 20 years total estimated benefits range from $16.7 million to $55.3 million.

Table 8 reports the total estimated net benefits associated with an average revision time of 1.5 years. Annualized over 20 years, total estimated net benefits range from $16.8 million to $54.7 million at a 3 percent discount rate, and from $16.4 million to $53.2 million at a 7 percent discount rate.

2. Medical Device Growth Rates

The above analysis assumes that there is no growth in medical device exports. However, changes in markets, regulations and technology could cause the export rate to increase or decrease. An increase in the rate with which companies export uniquely labeled medical devices would result in an increase in the total estimated net benefits associated with using stand-alone symbols, and vice versa. For instance, an increase in the export growth rate would result in an increase in the number of unique medical device labels in need of revisions to incorporate a new or changed symbol. The option to use stand-alone symbols would allow exporters to avoid the costs associated with revising the increasing number of separate U.S. only labels, which would result in an increase in total estimated net benefits. Estimating the export growth rate requires data that projects the

number of uniquely labeled medical devices that manufacturers are expected to sell in the future. Because these data are unavailable, we cannot quantify the extent to which changes in the growth rate would change the total estimated net benefits associated with using stand-alone symbols.

III. Regulatory Flexibility Analysis

FDA has examined the economic implications of the final rule as required by the Regulatory Flexibility Act. If a rule will have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities. We certify that this final rule is not expected to impose any new substantial burdens on small entities, and thus is not expected to impose a significant economic impact on a substantial number of small entities.

A. Description and Number of Affected Small Entities

The Small Business Administration (SBA) considers medical device manufacturers (NAICS codes 334510, 334517, 339112, 339113, 339114 and 339115) to be small when they employ under 500 workers (Ref. E3). The 2012 Economic Census provides the most currently available employment statistics (Ref. E4). The resource indicates that most medical device establishments are small: approximately 98 percent. However, this resource omits certain companies that are affected by the final rule, such as medical device relabelers, repackers and distributors. Some of these entities may be

exporters. Hence, our estimate may understate the actual number of small establishments and their respective cost savings.

B. Economic Effect on Small Entities

Table 9 reports the final rule's estimated impact on small entities. We approximate the estimated impact using percent costs per UPC: the ratio between unit labeling costs and revenues among small entities. To proxy unit revenues, we use the total value of shipments corresponding to the average medical device manufacturer within various size categories. Table 9 presents these values across three size categories, establishments that employ 0-19, 20-99 and 100-499 employees. The average value of shipments across these size categories—going from the smallest staff size to largest—is $3.3 billion, $12.6 billion and $57.4 billion, respectively. We estimate that the average percent costs per UPC are less than 0.01 percent. Hence, the agency concludes that this rule would not have a significant economic impact on any small entities.

TABLE 9—ESTIMATED IMPACT OF THE FINAL RULE ON SMALL BUSINESS ENTITIES

Establishments			Value of Shipments (in $1,000s)		Percent Cost per UPC of Average Value of Shipment		
Employees	Count	Percent	Total	Average	Low	Middle	High
0-19…….	4,333	67%	$ 3,305,672	$ 1,663	0.11	0.20	0.29
20-99……..	1,409	22%	$12,603,673	$ 12,914	0.01	0.03	0.04
100-499…..	714	11%	$57,353,355	$ 80,327	0.00	0.00	0.01

Notes—2012 Economic Census omits the value of shipments associated with 2,355 establishments employing 0-19 employees, and 433 establishments employing 20-99 employees. The value of shipments estimates correspond to the establishments that report value shipments data. Hence, the average value of shipments estimate of establishments employing 0-19 employees only corresponds to the 1,978 establishments that report value of shipments data.
Source: 2012 Economic Census (NAICS 325413, 334510, 334516, 334517, 339112, 339113, 339114, 339115)

The impact analysis indicates that companies can reap moderate cost-savings via switching to using stand-alone symbols under the final rule. On average, companies who

switch to using stand-alone symbols can expect to receive an average annual cost savings ranging from $500 to $1,500 per UPC. As a result, it is possible that providing medical device manufacturers with the option to use stand-alone symbols may encourage companies, including small companies, to either start exporting products or export more products.

IV. References

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E.2. U.S. Census Bureau, 2013 Annual Survey of Manufacturers," http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ASM_2014_31GS101&prodType=table, accessed May, 2015.

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E.6. Liu, L., U. Hoelscher, and T. Gruchmann. 2005. Symbol Comprehension in Different Countries: Experience Gained from Medical Device Area. *Mensch und Computer* pp. 81-87.

V. Appendices

A. Technical Appendix: Average Number of Uniquely Labeled Medical Devices by Establishment Size.

FDA assumes that the total number of uniquely labeled medical devices that U.S. companies use is approximately equal to the number of U.S. companies multiplied by the average number of devices they produce. However, larger establishments probably produce more uniquely labeled medical devices than smaller establishments, on average. Hence, to compute the total estimated number of uniquely labeled medical devices produced, we performed the following steps: first, we separated companies via size; second, we estimated the number of companies within each size category; third, we estimated the average number of uniquely labeled medical devices that companies produced within each size category; fourth, we took the product of these estimates within each size category; and finally, we summed the products.[1] We group manufacturers by size using the Census categorizations (Ref. E4). The Census groups companies together using their employee size; very small in size institutions employ 1-99 workers, small institutions employ 100-499 employees, and medium to relatively large in size institutions employ 500 or more workers.

[1] This estimation method may overstate the final rule's expected benefits. FDA guidance on "Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use" permits companies to use labels with certain stand-alone symbols on IVD devices intended for professional use. This caveat suggests that the approach may overstate the number of uniquely labeled medical devices that could be converted to labels with stand-alone symbols. However, IVD devices intended for professional use make up a modest portion of all uniquely labeled medical devices, suggesting that the method would modestly overstate the final rule's benefits.

To estimate the average number of uniquely labeled medical devices produced by different sized U.S. companies, FDA randomly sampled approximately 187 medical device manufacturers and collected the following data: the company's name, employee size, and the number of uniquely labeled medical devices available for purchase. Employee sizes are reported in manta.com and dnb.com. The number of uniquely labeled medical devices available for purchase was estimated via counting the total uniquely labeled medical devices in each company's product catalog, which includes any medical devices or medical device accessories registered with FDA. To illustrate the way we counted medical devices, we use an example. For instance, we considered pedicle screw systems and syringes as two separate uniquely labeled medical devices, while we considered syringes of varying colors and sizes as only one.

Table 10 presents the sample data. The table indicates that the random sample contains approximately 157 very small companies, 20 small companies and 10 medium large companies. On average, very small companies produce approximately 13.7 uniquely labeled medical devices, small companies produce 39.85 uniquely labeled medical devices, and medium to large companies produce 205.4 uniquely labeled medical devices.

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Very Small Companies: 1 - 99 Employees

Company Name	Uniquely Labled Medical Devices
3 Point Products	41
3 Test	3
A&D Medical Corp	12
Accell	4
Aci Medical	5
Acteon Satelec, Inc	7
Addto	3
Adhezion	2
AllStar Orthopedics & Medical Supplies, Inc	7
American Imex	42
AngioDynamics	20
AutomatedMedProducts	67
B & B Medical Technologies	17
BCI Dental Laboratories Inc	5
Belmont Instrument Corporation	12
Bertec	8
Bioclear	16
Biomeridian	3
Biowave Corp	5
Brasch Group	6
BridgePoint Medical, Inc.	2
Brymill	22
C L Sturkey Inc	1
Cadwell Laboratories	8
Cardia, Inc	5
Cardiocommand, Inc	6
Carolina Medical Electronics	2
Celo Nova	1
Centex Dental Lab	4
Ceplast Medical Devices LLC	1
Christy Manufacturing Company	1
Consensus Orthopedics	3
Convaid	31
Criticare Systems Inc	17
Cuda Surgical	17
CW Medical, Inc	15
Dental Arts Inc	7
Dentronix Inc	113
Dermlite	10
DGH	16
Dupaco Inc	4
Efficient Dental Technologies, LLC	5

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Very Small Companies: 1 - 99 Employees	
Company Name	**Uniquely Labled Medical Devices**
Elliquence LLC	10
Endocraft LLC	3
Eprt Technologies	3
Equip for Independence	1
Essential Dental Systems, Inc	8
Estill Medical Technologies, Inc	1
Eyenavision	3
Eyesys Vision Inc	2
Fem Suite LLC	2
FMD	1
Focus Medical, LLC	3
FutureMed America Inc	10
Gebaurer	5
Gereonics, Inc	1
Glenveigh Pharmaceuticals, LLC	3
Goldman Products, Inc	150
Great Laser	10
Griffin Laboratories	2
Highland Medical Equipment	5
Identure	1
IDEV	2
Imagederm Inc	4
Innovasis	6
InSightec, Inc.	6
Interrad Medical Inc	2
Ion Vision Inc	7
KBCO Inc	5
Key Surgical Inc	15
Konigsberg Instruments Inc	20
Kowa Optimed Inc	11
LAP of American LC	7
Laschal Dental Instruments, Inc	15
Laschal Surgical Instruments, Inc	8
Laser Engineerin, Inc	1
Laser Probe Inc	6
Lead Lok	8
Lhasa OMS	4

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Very Small Companies: 1 - 99 Employees	
Company Name	**Uniquely Labled Medical Devices**
LifeSciencePLUS	2
Maramed Orthopedic Systems	58
Mark Medical Manufacturing	111
Marpac	11
Medical Alignment Systems	2
Mediflex Surgical Products	202
Medyssey Co., Ltd	5
MHC Medical Products	8
Mimedx Group	4
Morrison Medical	85
Myerson L.L.C.	6
Myontronics Noromed, Inc	3
Neoforce group Inc	8
Neomedica Inc	7
Neuro Kinetics	3
Newmatic Medical	168
Ocular Systems Inc	1
Odyssey Medical	40
OmniLife Science	7
Optical Integrity, Inc	2
Optima Products Incorp	6
Orasure	5
Osseon Therapeutics Inc	4
Osstell Inc	1
Parcus Medical LLC	50
parksmed	24
Passy-Muir Inc	8
PMT Corp	32
Premier heart	1
QRS Diagnostic	8
Ranfac Corp	26
Redfield Corporation	1
Rehabtek LLC	2
River Rain Medical	2
Rocco's Originals	1
Saebo	3
Safe Stitch Medical Inc	5
Sagemax Bioceramics Inc	21
Salmon Medical Innovations LLC	1
Sciton	11
Scottcare Corporation	7
Secure Medical	1
Separation Technologies, Inc	1
Showcase Dental Lab	4
Signus Medical LLC	3

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Very Small Companies: 1 - 99 Employees	
Company Name	**Uniquely Labled Medical Devices**
Sooil Inc	4
Sooka Inc.	2
Stat Medical Devices	7
Sterigearm	1
Sun Medica	11
Sunoptic Technologies LLC	4
Sure Foot Inc	4
Surgiform	27
Suturtek	3
Syris Scientific LLC	2
ThermoTek Inc	12
Thibido Technology Inc	1
Tiba Medical Inc	1
Titan Spine LLC	5
Tracey Technologies Corp.	1
Trademark Medical	18
Translite LLC	4
Transmotion Medical Inc	10
Umbra Medical Devices	3
Uramix	2
US Therapy Inc	1
Varitronics Inc	7
Venni Instruments Inc	10
Vista Medical	3
Vita Needle Company	9
Westmed	80
World Trend, Inc	1
Wright Therapy Products	2
X-Spine	10
Z Medica	7
Zewa Inc	7
Ziemer USA	6
Zynex Medical	9
Average Exports	13.71428571

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Small Companies: 99 < Employees < 500

Company Name	**Uniquely Labled Medical Devices**
Animas Corp	2
Aseptico	63
Atrion Medical Products, Inc	2
Bio-Detek Inc	37
Burton Medical	24
Chad Therapeutics	5
Cutera	15
Dale Medical Products Inc	12
Dexcom	1
Jelco	19
King Systems Inc	60
Level 1	35
Lumitex	2
Medex	121
Mesa Laboratories, Inc.	15
Nonin	50
Portex	297
Propper Manufacturing CO Inc	30
Therma Solutions	1
Verathon	6
Avg Exports	39.85

TABLE 10—ESTIMATED AVERAGE NUMBER OF UNIQUELY LABELED MEDICAL DEVICES

Medium to Large Companies: 500 + Employees

Company Name	**Uniquely Labled Medical Devices**
3M	120
Airlife	190
ArthroCare ENT	10
Bard Davol	75
Bio-Detek Inc	37
Covidien	337
Johnson & Johnson	850
Physio Control	136
WelchAllyn	207
Xltek	92
Avg Exports	205.4