

Mandates Reform Act of 1995 requires that agencies prepare a written assessment of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year (adjusted annually for inflation).

We believe that this final rule is consistent with the regulatory philosophy and principles identified in Executive Order 12866 and in these two statutes. The final rule is a significant regulatory action as defined in section 3 paragraph (f)(4) of the Executive order. However, as shown in this section VIII, the final rule will not be an economically significant regulatory action as defined by the Executive order and will not require further analysis under the Regulatory Flexibility Act.

The Unfunded Mandates Reform Act of 1995 does not require FDA to prepare a statement of costs and benefits for the final rule because the final rule would not result in an expenditure of \$100 million in any one year, adjusted for inflation. The current inflation-adjusted statutory threshold is approximately \$110 million.

The purpose of this final rule is to require applicants to submit in electronic format the content of labeling required under § 201.100(d)(3) in NDAs, ANDAs, BLAs, annual reports, and applicable supplements. Submissions in electronic format will help simplify and speed up our review of these documents. Currently, applicants may voluntarily submit such data in electronic form, but they are not required to do so. The rule will require all applicants of approved and new NDAs, BLAs, and ANDAs to convert the content of labeling to an electronic format for submission. At this time, PDF is the type of electronic file format that we have the ability to accept for processing, reviewing, and archiving. Applicants that do not already have the capabilities to create PDF files will have to acquire the software and expertise to do so or make contractual arrangements to have documents converted.

The economic burden on industry will include a one-time cost to acquire the appropriate computer software and train employees on its use. Applicants may also incur additional one-time costs to revise applications that have not had any labeling changes within the last few years to a format that can be converted to a PDF file. We do not know the number of applicants that currently have the capability to submit electronic files, nor do we have firsthand information on how labeling files are currently maintained or on how much

time will be required to train employees on the software and new procedures.

Three comments were received regarding the economic impact analysis. Two of these comments suggested that the cost to convert the content of labeling to a PDF format was underestimated because it did not include the cost to proofread the labeling after it is converted to a PDF file. The time required for proofreading ranged from 4 to 6 hours depending on the complexity/length of the labeling. One of these comments also suggested that the cost for converting older labeling that is only available on paper was underestimated, suggesting that the costs should include costs for equipment, training, and time to scan paper documents.

The agency agrees that we should allow for proofreading of labeling under certain circumstances. Applicants that have previously submitted annual reports or supplements in paper form, but also maintained the documents in electronic format, should be provided time for proofreading the converted file. This category of labeling would not require any changes to the labeling since it was last submitted to the agency. It only requires additional time for proofreading to ensure that it is the same as the labeling submitted in paper format. Five hours was used in this analysis to reflect the cost under these circumstances.

However, we do not agree that proofreading is an incremental cost for labeling that has been changed and is in a word processing file. Proofreading of the finished product for submission (in this case, the PDF file) is done now as part of current industry quality assurance practice. We also do not agree with the comment that costs for scanning labeling should be included in the impact analysis. While scanning paper labeling and using optical character recognition software is an option some firms may choose, it is not required. The labeling can be transcribed into a word processing format and then converted. However, we did increase the time estimate for such conversions by an additional 2 hours and we also increased our estimate of the percent of labeling that is included in this category because we now believe that number was underestimated.

Annually, we receive approximately 425 applications, 7,125 annual reports, and 1,650 supplements that contain labeling from approximately 625 applicants. Based on our experience working with voluntary electronic submissions, we estimate that overall approximately 70 percent of the

applicants (440) already have the necessary software and trained personnel to comply with this rule. The remaining 30 percent of applicants (190) would need to purchase software, which costs about \$250. Based on agency review, approximately 78 percent of these 190 applicants 148 would be considered small (fewer than 750 employees for drug product manufacturers and fewer than 500 employees for biological product manufacturers). We estimate that each small applicant would need to purchase only one copy of the software, for a total of 148 copies. The remaining 22 percent of applicants (42) that would need to purchase software are large entities. The agency estimates that each of these firms would need to purchase about 3 copies of the software or 126 copies (42 x 3). Thus, the total one-time cost for software is \$68,500 ((148 + 126) x \$250). Training costs include the cost of the software training course (estimated at \$150 for a 6-hour course) and the wages of the employees attending the course (assuming an average weighted wage rate of \$40 per hour). We estimate that applicants would train two employees per software purchase (548 employees), for a total one-time cost of \$213,720 (((\$150 + (6 hours x \$40)) x 548). The total one-time cost for software and training combined is estimated to be \$282,220 (\$68,500 + \$213,720).

The cost to convert the applicable labeling to an electronic format is a one-time cost. The cost of conversions for new NDAs, BLAs, and ANDAs will be nominal because the file would be in a format easily convertible to PDF. The PDF file, being the finished product, would be proofread for quality assurance. Annually, we receive approximately 1,650 supplements that would be subject to the final rule. Because the majority of products for which supplements are submitted would have had labeling changes within the last few years, most labeling files would be easily accessible. Currently, the labeling in about 40 percent (660) of the supplements received is submitted in a PDF format and would require an estimated additional 15 minutes to comply with this final rule. The labeling in the remaining 60 percent (990) will require an estimated 5 hours to process and proofread. Thus, the total number of hours needed to convert applicable labeling in supplements to a PDF file format is 5,115 ((0.25 x 660) + (5 x 990)).

Labeling in most of the annual reports will also need to be converted. The conversion of this labeling to a PDF file for about 40 percent of NDA annual reports (975), 50 percent of ANDA annual reports (2,295), and 40 percent of