

drug being blocked for a typical period of time. We estimated the 1-year loss in innovator revenues to be \$3.160 billion. As discussed in the proposed rule, we believe that the negative impact on innovators from earlier generic competition will be mitigated somewhat by a reduction in required innovators' costs. With earlier generic competition, innovators will reduce marketing expenses. In the proposed rule, we estimated the 1-year reduction in support costs to be approximately \$142 million. For the final rule, we estimate that the 1-year loss in revenues, after adjusting for the reduction in support costs, is \$3.017 billion, the same as in the proposed rule.

2. Declaration Costs

In the proposed rule, we used earlier information collection data to estimate there will be 124 annual patent declarations by innovator firms. We now believe that the number of patents submitted to us each year would better estimate the annual number of patent declarations. For the years 1998 to 2002, the numbers of patents submitted to us were 159, 205, 321, 280, and 268 respectively, for an annual average of 246. We understand that many of these individual patents are included in multiple NDA submissions, so there could be multiple declarations for a single patent and this method could underestimate the number of declarations. From our review of submissions, we believe the number of duplicate patent listings to be 20 percent of the number of unique patents. Therefore, we estimate 49.2 (246.6×20 percent) patent declarations will be multiple listings, and there will be 295.8 ($246.6 + 49.2$) annual patent declarations. We have created patent declaration forms to make the submission of patent information less burdensome. The two forms, for filing with an NDA submission and upon or after NDA approval, will contain more information, but we have simplified the format to make these easier to complete. In simplifying the forms, we believe our initial estimate of 24 additional hours per declaration to complete these forms likely overstates the actual burden. To account for the simplification of the declaration process, we have lowered the expected time required to complete a patent declaration to 18 hours.

A regulatory affairs specialist could perform the tasks associated with this process. Based on the total average hourly compensation of \$55.14² the

estimated cost would be \$992 ($\55.14 per hour \times 18 hours) per event. The burden on individual firms would depend on the number of declarations they submit. We estimate that the 1-year burden for submitting patent declaration forms is \$293,000 ($\992 per event \times 295.8 events).

3. Cost of Submitting Polymorph Patents

We are requiring the submission of patent information for patents that claim different polymorphs of the active ingredient described in the NDA. NDA holders will now be able to submit these polymorph patents for listing in the Orange Book, as long as they have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA.

We cannot make a precise estimate of the impact of these requirements, as costs can vary substantially depending on the substance being tested, the number of subjects required, the cost of raw materials, and other factors. As part of an unrelated study in 1998, we commissioned a contractor, Eastern Research Group (ERG) to estimate the cost of bioequivalence testing. We believe the burden of demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA to be similar to that of demonstrating bioequivalence. Our estimates include both the cost of manufacturing the batch and the cost of conducting the bioequivalence testing. ERG found the cost of performing such testing to be between \$70,000 and \$750,000.³ We believe the cost of showing "sameness" to be at the higher end of this range, and estimate the burden to be between \$500,000 and \$750,000. The midpoint of this estimate is \$625,000. (We did not adjust the ERG estimates for inflation.)

We believe a firm's decision to submit a polymorph patent for listing will depend on whether the expected benefits to the firm from listing exceed the costs of showing "sameness." We recognize that potential benefits from listing polymorph patents may be reduced by the elimination in the final rule of multiple 30-month stays in approval of ANDA or 505(b)(2) applications. Thus, the cost of demonstrating "sameness" would deter submitting patents for listing with expected values less than approximately

² then adjusted for inflation at 1.58 percent (unadjusted CPI-U) and increased 40 percent to account for benefits.

³ Pharmaceutical Industry Cost Savings Through Use of the Scale-up and Post-Approval Change Guidance for Immediate Release Solid Oral Dosage Forms (SUPAC-IR), prepared for FDA, 1998, p. 63.

\$625,000. We believe the typical value of a deterred polymorph patent to be substantially less than the cost of submission of the patent for listing, as many of the patents have little value without the ability to delay generic entry through multiple 30-month stays. For this analysis, we assume such low value patents to be worth approximately 20 percent of the cost of showing "sameness," or \$125,000.

We believe the annual number of polymorph patents that will be submitted for listing to be small, but we do not know with certainty. We reviewed a publicly available listing of NDAs in which an outside party had identified patents it judged to be polymorph patents. Of the 105 NDAs in the sample, there were 13 polymorph patents. Applying that same ratio to the 107 expected NDAs per year, we estimate 13.2 ($107 \times 13 / 105$) potential polymorph patents to be submitted for listing per year. We assume that a polymorph patent will have a high potential value (greater than \$625,000—the midpoint of the testing cost estimates) and be submitted, or will have a low potential value (\$125,000) and not be submitted. With the elimination of multiple 30-month stays per ANDA or 505(b)(2) application, we believe the number of high-value polymorph patents to be a subset of the number of total polymorph patents, and assume three-fourths of the potential patents will not be submitted for listing. Thus, we assume 3.3 (13.2 potential patents \times 0.25 likelihood of being high value) patents will be submitted for listing at a 1-year cost of \$2.06 million (3.3 patents \times \$625,000 cost per patent). Likewise, we assume 9.9 (13.2 potential patents \times 0.75 likelihood of being low value) patents will not be submitted each year. We estimate the 1-year cost from the inability to submit these patents for listing to be \$1.24 million (9.9 patents \times \$125,000 value of low-value patent) and the 1-year burden associated with the test data demonstrating "sameness" for polymorph patents to be submitted for listing is estimated to be \$3.3 million ($\2.06 million $+$ $\$1.24$ million).

4. Total Costs of the Regulation

The total costs of the final rule include the lost revenues to innovator firms from the erosion of market share, mitigated by the decrease in support costs, the cost of completing a more detailed patent declaration, and the costs associated with the requirement that test data exist demonstrating "sameness" in order to submit a polymorph patent for listing. The estimated 1-year loss in revenues from

² The figure of \$55.14 represents the hourly rate for "lawyer" from the Bureau of Labor Statistics 2003 National Compensation Survey of \$38.77, and