DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Postmarketing Safety Reports for Approved New Animal Drugs; Electronic Submission Requirements

Docket No. FDA-2017-N-6381

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

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Office of Economics and Analysis
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## I. Introduction and Summary

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, Executive Order 13771, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us 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). Executive Order 13771 requires that the costs associated with significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations." We believe that this final rule is not an economically significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the costs of the rule are minimal in both absolute value and in comparison to average yearly sales of small firms in this industry we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing "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 $156

million, using the most current (2019) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

The purpose of this rule is to require electronic submission of certain postmarketing safety reports for approved new animal drugs. The rule would also provide a procedure for requesting a temporary waiver of the electronic reporting requirement for "good cause" shown, such as a natural disaster. This rule would not change the content of the postmarketing safety reports or the frequency of the reporting requirements.

Currently, most submitters have chosen, voluntarily, to use electronic submission for the reports that would be affected by this final rule. As of 2016, 99.7 percent of postmarketing safety reports eligible for electronic submission were electronically submitted. Thus, this final rule would affect a small proportion of these reports.

## A. Summary of Costs and Benefits

The quantifiable benefit of this rule is annual cost savings of $5,259 from reduced data entry time for the Center for Veterinary Medicine (CVM). The other benefits of this final rule would be to animal health and are not quantifiable.

The main cost to this rule is a one-time upfront cost to industry of $73,500 for changing standard operating procedures (SOPs) and training employees to electronically submit postmarketing safety reports in accordance with the new SOPs. Recurring costs to the Food and Drug Administration (FDA or Agency) would be $161 per year, for processing the waivers to the electronic reporting requirement. Annualizing these costs over a 15-year time horizon (from 2018 to 2033), we estimate total annualized costs to be $6,139 at a 3 percent discount rate, and total

annualized costs of $7,703 at a 7 percent discount rate. The annualized net benefit of this rule is -$880 at a 3% discount rate and -$2,444 at a 7% discount rate. The present value of the net benefits is -$10,504 at a 3% discount rate and -$22,262 at a 7% discount rate over a 15-year time horizon.

Table 1. Summary of Benefits and Costs in 2017 Dollars Over a 15-year time Horizon

| Category | | Primary Estimate | Low Estimate | High Estimate | Units | | | Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | Year Dollars | Discount Rate | Period Covered | |
| Benefits | Annualized Monetized $/year | $5,259 | | | 2017 | 7% | 15 | |
| | | $5,259 | | | 2017 | 3% | 15 | |
| | Annualized Quantified | | | | | 7% | | |
| | | | | | | 3% | | |
| | Qualitative | | | | | | | |
| Costs | Annualized Monetized $/year | $7,703 | | | 2017 | 7% | 15 | |
| | | $6,139 | | | 2017 | 3% | 15 | |
| | Annualized Quantified | | | | | 7% | | |
| | | | | | | 3% | | |
| | Qualitative | | | | | | | |
| Transfers | Federal Annualized Monetized $/year | | | | | 7% | | |
| | | | | | | 3% | | |
| | From/ To | From: | | | To: | | | |
| | Other Annualized Monetized $/year | | | | | 7% | | |
| | | | | | | 3% | | |
| | From/To | From: | | | To: | | | |
| Effects | State, Local or Tribal Government: | | | | | | | |
| | Small Business: | | | | | | | |
| | Wages: | | | | | | | |
| | Growth: | | | | | | | |

In line with Executive Order 13771, in Table 2 we estimate present and annualized values of costs and cost savings over an infinite time horizon. Based on these cost-savings this final rule would be considered a deregulatory action under EO 13771. Our primary estimate for the present value of the net costs over an infinite time horizon is -$3,837 (or a cost savings of $3,837) at a 7% discount rate and -$96,287 at a 3% discount rate in 2016 dollars.

Table 2. EO 13771 Summary Table (in 2016 Dollars, Over an Infinite Time Horizon)

| | Primary (7%) | Lower Bound (7%) | Upper Bound (7%) | Primary (3%) | Lower Bound (3%) | Upper Bound (3%) |
|---|---|---|---|---|---|---|
| Present Value of Costs | $69,720 | | | $75,346 | | |
| Present Value of Cost Savings | $73,557 | | | $171,634 | | |
| Present Value of Net Costs | ($3,837) | | | ($96,287) | | |
| Annualized Costs | $4,880 | | | $2,260 | | |
| Annualized Cost Savings | $5,149 | | | $5,149 | | |
| Annualized Net Costs | ($269) | | | ($2,889) | | |

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule [1] and at *https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm*

## B. Comments on the Preliminary RIA and Our Responses

In 2018, FDA published the proposed rule "Postmarketing Safety Reports for Approved New Animal Drugs; Electronic Submission Requirements" [2]. We prepared a comprehensive preliminary regulatory impact analysis for the 2018 proposed rule [1]. We received no comments on our analysis.

## C. Summary of Changes

Only minor changes were made to the Proposed Regulatory Impact Analysis (PRIA). We have updated all wages used in the calculations to reflect 2017 wage rates.

## II. Final Regulatory Impact Analysis

### A. Background

Postmarketing safety reports are an important resource for FDA. These reports are the primary means by which we obtain information regarding problems with the safety or effectiveness of marketed approved new animal drugs, as well as product or manufacturing problems [3]. The reports include information regarding suspected adverse events, such as: date, drug, type of animal affected (including specific animal characteristics), reporter, whether the drug was used on label or in an extralabel manner, and a detailed description of the adverse event. These adverse events and product or manufacturing problems are typically reported to the applicant or nonapplicant[1] by the animal's owner or the treating veterinarian. The reports sent by the applicant or nonapplicant to CVM or the proper FDA District Office or local FDA resident post for review and assessment.

#### 1. Reports affected by this rule

There are several post marketing safety reports that would be affected by this final rule (See Table 3). First, the three-day alert report that must be submitted by applicants. Currently, this report must be submitted on paper to the FDA District Office or local FDA resident post, but an additional copy may also be submitted on paper or electronically directly to CVM. The rule would require that any optional additional copies submitted directly to CVM be submitted electronically.

[1] An applicant is defined as "a person or entity who owns or holds on behalf of the owner the approval for an NADA [new animal drug application] or an ANADA [abbreviated new animal drug application], and is responsible for compliance with applicable provisions of the act and regulations." (§ 514.3 (21 CFR 514.3)) A nonapplicant, is defined in § 514.3 as "any person other than the applicant whose name appears on the label and who is engaged in manufacturing, packing, distribution, or labeling of the product."

Second, the fifteen-day alert report currently must be submitted to CVM on paper or electronically. This rule will require that these reports must be submitted electronically.

Third, the nonapplicant reports currently must be submitted by nonapplicants to the applicant, but additional copies may be submitted to the Agency either electronically or on paper. This rule would require that if the additional copies are submitted to CVM that they are electronic.

Fourth, Reports of product/manufacturing defects and adverse drug experiences submitted as part of the periodic drug experience report may currently be submitted in paper or electronic form. This rule will be require them to be submitted electronically.

The rule would also create a procedure for requesting from CVM a temporary waiver of the electronic reporting requirement for "good cause" shown (e.g., a natural disaster that makes electronic submission impossible).

Table 4. Summary of Affected Reports

| Report | Current Requirements | Requirements Under this Rule* |
|---|---|---|
| Three-day alert reports (§ 514.80(b)(1)) | Must submit a report to the appropriate FDA District Office or local resident post on *paper*. May also submit a copy to the Agency on *paper or electronically*. | Must submit a report to the appropriate FDA District Office or local resident post on *paper*. May also submit a copy to the Agency *electronically*. |
| Fifteen-day alert reports (§ 514.80(b)(2)(i)) and followup reports (§ 514.80(b)(2)(ii)) | Must be submitted on *paper or electronically* to the Agency. | Must be submitted *electronically* to the Agency. |
| Nonapplicant reports (§ 514.80(b)(3)) | Nonapplicants are required to forward reports of adverse drug experiences to the applicant. A nonapplicant may choose to also submit an additional report directly to the Agency on *paper or electronically.* | Nonapplicants are required to forward reports of adverse drug experiences to the applicant. A nonapplicant may choose to also submit an additional report directly to the Agency *electronically*. |
| Reports of product/manufacturing defects and adverse drug experiences submitted as part of the periodic drug experience report (§ 514.80(b)(4)(iv)(A) and (C)) | Applicants are required to submit this report periodically either on *paper or electronically.* | Applicants are required to submit this report periodically *electronically*. |

*Temporary waivers can exempt firms from electronic reporting requirements.

## B. Market Failure Requiring Federal Regulatory Action

This regulation addresses market inefficiencies caused by a principal-agent problem. In a principal-agent problem, the agent can make decisions that impact the principal without taking the principal's interests or the overall market efficiency into account. In this case, the agents are those firms submitting reports to CVM. The ability to submit paper reports may be more efficient for the agent, as it negates the potentially costly need to re-write standard operating procedures (SOPs). The majority of firms already choose to submit electronically, so it was efficient for most firms to switch. The ability of agents to submit paper forms to CVM causes market inefficiencies because it imposes the cost of dealing with paper forms on the principal, CVM, and slows the transfer of information. With paper forms CVM must commit more employee time to entering and reviewing the information than with electronic forms. Manually entering the information can take several weeks causing significant slowdowns for CVM to review, assess, and make a determination on the potential for new issues. Requiring these forms be submitted electronically will fix the market inefficiency.

## C. Purpose of the Rule

The purpose of this rule is to require the electronic submission of certain postmarketing safety reports for approved new animal drugs. The rule would also establish a new procedure for requesting a temporary waiver of the electronic reporting requirement, which would allow paper submissions for a "good cause." The rule affects all groups (i.e., both applicants and nonapplicants) required to submit postmarketing safety reports under §§ 514.80(b)(1), 514.80(b)(2)(i), 514.80(b)(2)(ii), 514.80(b)(3), 514.80(b)(4)(iv)(A), and 514.80(b)(4)(iv)(C) of the Federal Food, Drug, and Cosmetic Act. This rule will not change the contents of these postmarketing safety

reports or the frequency of the required reporting. These reports are submitted to CVM, FDA District Offices, or local FDA resident posts.

## D. Baseline Conditions

Currently, the majority of submitters have voluntarily chosen to use electronic submission for the postmarketing safety reports that would be affected by this rule. In calendar year 2016, 99.7% of all postmarketing safety reports eligible for electronic submission were voluntarily submitted electronically. (Table 3) The rule would therefore only affect 0.3% (270) of the reports currently submitted on paper. (This does not include the voluntarily submitted additional copies of the 3-day field reports.) From 2011 – 2015, only 15 companies submitted paper reports. This rule, therefore, would affect only a small number of entities and a small proportion of total reports.

From 2015 through 2016, the number of reports that were submitted on paper dropped significantly. This was due primarily to two factors: (1) some large companies, which submit a large number of reports, switched to completely electronic reporting; and (2) some industry consolidation, whereby larger firms (that submit electronically) bought smaller firms (that may have historically submitted on paper), and all subsequent reports by the new company were submitted electronically. Because we believe that these market changes are permanent, we use the number of 2016 paper reports for this analysis, rather than an average, as the baseline number of reports affected by the rule.

Table 5. Summary of the Baseline Conditions

| 21 CFR Section or Section of the Act | FDA Form Number | Affected by the Rule | CY2014 | CY2015 | CY2016 |
|---|---|---|---|---|---|
| 514.80(b)(1) | 3-day Field Alert Report 1932 (Paper) | No | 225 | 302 | 337 |
| 514.80(b)(1) | 3-day Field Alert Report 1932 (Additional "Courtesy" Copy) | Yes | 18 | 114 | 95 |
| 514.80(b)(2)(i) and (ii) And 514.80(b)(3), together | 1932 (Electronic) | No | 38,300 | 41,673 | 47,978 |
| 514.80(b)(4) | 1932 (Electronic) | No | 49,419 | 45,389 | 50,850 |
| 514.80(b)(2)(i) and (ii) And 514.80(b)(3) together | 1932 (Paper) | Yes | 125 | 242 | 93 |
| 514.80(b)(4) | 1932 (Paper) Accompanying 2301 | Yes | 1570 | 1059 | 177 |

For this analysis, we estimate the costs and benefits of the rule associated with moving from paper reports to electronic reports. However, we do not include the optional additional 3-day field reports in the analysis. We exclude these reports because they are optional copies, and the rule does not change their reporting status (it only mandates that, if submitted, they must be submitted electronically). We assume that firms using paper reporting will simply stop sending additional copies, rather than incurring the costs of switching to electronic reporting. Because of the optional nature of these reports, we assume this change will incur no additional costs or benefits to firms or FDA.

## E. Benefits of the Rule

### 1. Non-quantifiable Benefits

By requiring electronic submission, FDA expects benefits from increasing the speed at which CVM is able to review, identify, and analyze new postmarketing events. This increased speed could reduce the time it takes to identify any new safety, efficacy, or manufacturing problems. The change would assist CVM in more rapidly reviewing postmarketing safety reports,

identifying emerging safety problems, and disseminating safety information in support of the public health mission. Accordingly, this should increase the potential health and safety of animals. In addition, the amendments would facilitate international harmonization and exchange of safety information. While these are important benefits of the rule, they are difficult to quantify.

2. Quantifiable Benefits

Though the health and safety benefits of this rule are difficult to quantify there are quantifiable cost savings. Electronic submissions removes CVM's need to input the data from paper submissions into the electronic system. These cost-savings include: reducing the cost of physically handling the paper reports; reducing the cost of manually entering the data from them into the electronic database; and reducing the possibility of errors that can occur during data entry. Resources that are now used to handle paper reports and manually enter the data could be redirected to other public health initiatives.

CVM received 270 postmarketing safety reports that would be affected by this rule in 2016. The primary costs for handling paper reports and entering the data from them into the electronic database are the costs of the Document Control Unit employee time and the data entry contractor time. We estimate that to register, copy, triage, and route a paper report takes a Document Control Unit employee 10 minutes longer per report than for an electronically submitted report. We also estimate that it takes a data entry contractor, on average, 15 minutes to enter the data from a paper report into our electronic database, which is unnecessary for electronically submitted reports.

To estimate the cost savings of the time no longer spent processing paper reports, we first estimate the costs of each type of employee. Using data of employees in the Document Control Unit, we estimate their wage rate to be $35 per hour. We double this wage estimate to account for benefits and overhead, resulting in a wage rate of $70 per hour. We estimate the cost of a data

entry contractor according to the Bureau of Labor Statistics (BLS) estimate of the average hourly wage for Data Entry and Information Processing Workers (occupation code 43-9020) in Sector 62 – Health Care and Social Assistance and double the wage to account for benefits and other overhead [4]. The BLS hourly wage estimate is $16; doubling the wage to account for fringe benefits and overhead, we estimate that the average hourly cost of a data entry contractor to process the paper reports is $31.

Using the 2016 estimate of 270 paper reports, we calculate the expected annual cost savings of the rule due to decreased costs of processing paper reports to be $5,259 =((270*($70/6))+(270*($31/4)). Accrued over 15 years, the present discounted value of the cost savings of this rule is $62,778 at a 3% discount rate and $47,896 at a 7% discount rate.

## F. Costs of the Rule

There are two main monetized costs associated with this final rule. First, there is the one-time cost to firms to comply with the rule. This cost includes both the cost of creating new SOPs to submit the reports electronically and the cost of training employees to electronically submit postmarketing safety reports in accordance with the new SOPs. We estimate that there would be no annually recurring costs to firms because this final rule would not change the contents of these postmarketing safety reports or the frequency of the required reporting. The second cost of the rule is the annual cost to FDA to administer a temporary waiver of the electronic submission requirement.

FDA estimates that approximately 15 firms would be affected by this rule. This estimate is based on the number of firms that, from 2011 – 2015, submitted a paper postmarketing safety

report to CVM. We use this estimate of 15 affected firms when calculating the cost of complying with this rule.

1. Costs to Industry

To estimate the one-time cost to firms of complying with this rule, we must calculate two separate costs. First, we calculate the cost of creating new SOPs, and we then calculate the cost of training employees to electronically submit postmarketing safety reports to CVM in accordance with the new SOPs. We assume that there are no capital costs associated with firms implementing this rule (i.e., firms in the pharmaceutical industry already have the computer and internet capacity necessary to electronically submit postmarketing safety reports).

We expect it will take approximately 20 hours per firm to create new SOPs for electronic submission of postmarketing safety reports [5]. We estimate this cost using the industrial production manager (code 11-3051) in NAICS 325400 – Pharmaceutical and Medical Manufacturing industry which has a mean hourly wage rate of $61.35 or a fully loaded wage rate of $123 per hour [6]. Therefore, we calculate the per firm cost of creating SOPs to be $2,023; adjusting to 2016 dollars, this becomes $2,450. With an estimated 15 firms being affected by the rule, we estimate a total one-time cost of creating new SOPs to be $36,750.

The second cost to firms for complying with this rule is associated with training employees to electronically submit postmarketing safety reports in accordance with the new SOPs. We estimate the time per firm to complete this training to also be 20 hours, with the main cost being the time employees spend in this training. We use the hourly wage (plus benefits and overhead) of the trainer, who we assume to be the same person who would create the SOP, to proxy for the

value of all employee time. Therefore, we estimate the per firm cost of employee training to be $2,450, and the total one-time cost of training for all 15 affected firms to be $36,750.

Based on these two cost estimates, we estimate that the total one-time costs to firms to implement this rule would be $73,500, with an average one-time cost per firm of $4,900.

2. Costs of reviewing waiver

There are also costs to FDA associated with this rule. CVM will need to create and administer a waiver process for accepting paper reports on a limited basis. CVM estimates that there would be no more than one waiver request per year, which would take 1.25 hours for staff to review. Assuming an FTE FDA employee cost (salary, plus benefits and overhead) of $129 per hour, the annual cost of administering the waiver program would be approximately $161. There would also be some diminishment of benefits (in terms of the incremental reduction due to processing paper reports) because of this waiver process. However, the total reduction in benefits would depend on the number of paper reports submitted during the timeframe covered by a waiver. Because we estimate that requests for a waiver would be rare, and because of the uncertainty of how many paper reports would be submitted during any waiver period, the potential reduction in benefits due to waivers is not estimated here.

Table 6. Costs of the Final Rule (in 2016 dollars)

| Cost Type | Year 1 Costs | Year 2 and Each Subsequent Year Costs |
|---|---|---|
| For Firms | | |
| SOP Creation (one-time) | $36,750 | |
| Training (one-time) | $36,750 | |
| | | |
| For FDA | | |
| Waiver Process (annual) | $161 | $161 |
| | | |
| Total | $73,661 | $161 |

## G. Summary of Costs and Benefits

The principal unquantified benefit of this final rule would be the animal health benefits associated with more rapid processing and analysis of postmarketing safety reports submitted on paper.

The principal quantified cost saving of this final rule is the expected annual cost savings to FDA of $5,259 due to decreased costs of physically handling paper reports and manually entering the data from them into the electronic database.

The total one-time costs to affected industry are creating new SOPs and training employees to electronically submit postmarketing safety reports to CVM in accordance with the new SOPs, and are estimated at $73,500. The annual cost to FDA of administering the waiver process is estimated at $161. Additional costs to FDA of processing the paper reports during a waiver period are not quantified, due to uncertainty surrounding the number of reports that may be submitted.

Table 7. Summary of the Costs and Benefits of the Final Rule (in 2017 dollars)

| Effect | Year 1 Effects | Year 2 and Each Subsequent Year Effects | Annualized Over a 15-Year Period | |
|---|---|---|---|---|
| Costs | | | 3% discount rate | 7% discount rate |
| For Firms | | | | |
| SOP Creation | $36,750 | - | $2,989 | $3,771 |
| Training | $36,750 | - | $2,989 | $3,771 |
| | | | | |
| For FDA | | | | |
| Waiver Process | $161 | $161 | $161 | $161 |
| | | | | |
| Total | $73,661 | $161 | $6,139 | $7,703 |
| | | | | |
| Cost Savings | | | | |
| FDA Costs Savings from More Efficient Report Processing | $5,259 | $5,259 | $5,259 | $5,259 |

## H. Distributional Effects

We do not expect there to be any distributional effects from this rule.

## I. International Effects

We do not expect there to be any significant quantifiable international economics effects of this rule. One of the goals of the rule is to facilitate international harmonization and exchange of safety information. Therefore, the electronic reporting may increase other countries utilization of our safety information and help to identify potential issues sooner.

## J. Regulatory Alternatives

The rule finalizes a 12-month compliance period. In this analysis, we consider two alternative regulatory approaches: requiring compliance with the rule within 6 months and requiring compliance within 18 months. It is expected that shortening the timeframe for compliance with the rule would allow the benefits of the rule to accrue earlier. However, cost to firms would increase, although this increase is not substantial. (Table 6)

Lengthening the timeline for compliance would decrease costs to firms by allowing more time to implement new SOPs associated with the rule. However, this decrease is also not substantial (Table 7). Lengthening the compliance period would also delay the quantified benefits of the rule.

Table 8. Changes to the Costs & Cost Savings of the Final Rule Under a 6-month Regulatory Compliance Period (in 2017 dollars)

| | Present Value | | Annualized Costs Over a 15-Year Period | |
|---|---|---|---|---|
| | 3% discount rate | 7% discount rate | 3% discount rate | 7% discount rate |
| Costs | | | | |
| 6-month compliance period | $74,373 | $72,572 | $6,230 | $7,968 |
| Difference from 12-month compliance period | $1,091 | $2,414 | $91 | $265 |
| | | | | |
| Cost Savings | | | | |
| 6-month compliance period | $63,713 | $49,544 | $5,337 | $5,440 |
| Difference from 12-month compliance period | $935 | $1,648 | $78 | $181 |

Table 9**.** Changes to the Costs & Cost Savings of the Final Rule Under an 18-month Regulatory Compliance Period (in 2017 dollars)

| | Present Value | | Annualized Costs Over a 15-Year Period | |
|---|---|---|---|---|
| | 3% discount rate | 7% discount rate | 3% discount rate | 7% discount rate |
| Costs | | | | |
| 18-month compliance period | $72,207 | $67,825 | $6,049 | $7,447 |
| Difference from 12-month compliance period | ($1,075) | ($2,334) | ($90) | ($256) |
| | | | | |
| Cost Savings | | | | |
| 18-month compliance period | $61,857 | $46,303 | $5,182 | $5,084 |
| Difference from 12-month compliance period | ($921) | ($1,593) | ($77) | ($175) |

Note: Numbers in parentheses denote a reduction relative to the final rule impacts.

## III. Final Small Entity Analysis

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the costs of the rule are minimal in both absolute value and in comparison to average yearly sales of small firms in this industry we certify that the final rule will not have a significant economic impact on a substantial number of small entities. This analysis, as well as other sections in this document, serves as the Final Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

### K. Description and Number of Affected Small Entities

The Small Business Administration defines an entity in the pharmaceutical industry as small if it has fewer than 1,250 employees [7]. This includes entities classified under North American Industry Classification System (NAICS) code 325411. We estimate that up to 15 firms would be affected by this final rule. (From 2011 – 2015, 15 firms submitted at least one postmarketing safety report in paper format.) To determine whether these firms are small businesses, we analyzed the number of employees that each firm had using Dun & Bradstreet. We found that 11 of these firms would be considered small businesses under the Small Business Administration definition.

### L. Description of the Potential Impacts of the Rule on Small Entities

The one-time costs of implementing this rule per firm was estimated at $4,900. Of the 11 small business firms that may be affected by this rule, for which Dun & Bradstreet had sales data, the mean yearly sales per firm is $42 million (minimum of $104,000 and maximum of $222 million). If we further restrict this to firms with 10 or fewer employees, or those firms listed as having less than $1 million in yearly sales, the mean yearly sales are approximately $415,000. This implies that the one-time costs of implementing the rule are 1.2 percent of sales ($4,900/$415,000

= 0.012, or 1.2 percent). Because these are one-time fixed costs that are not incurred each year, we certify that this rule will not have a significant impact on a substantial number of small entities.

### M. Alternatives to Minimize the Burden on Small Entities

Because the estimated one-time costs per firm are low, even in comparison with annual revenues, we certify that this rule will not have a significant economic impact on a substantial number of small entities.

## IV. References


[1] Economics Staff, "Preliminary Regulatory Impact Analysis: Postmarketing Safety Reports for Approved NewAnimal Drugs; Electronic Submission Requirements," Food and Drug Administration, 2018.

[2] Center for Veterinary Medicine, "Postmarketing Safety Reports for Approved New Animal Drugs; Electronic Submission Requirements: Proposed Rule," Food and Deug Administration, Silver Spring, 2018.

[3] Food and Drug Administration, "Veterinary Adverse Event Reporting for Manufacturers," Food and Drug Administration, 22 February 2018. [Online]. Available: https://www.fda.gov/AnimalVeterinary/SafetyHealth/%20ReportaProblem/ucm212682.htm. [Accessed 14 August 2018].

[4] Bureau of Labor Statistics, "May 2017 National Industry-Specific Occupational Employment and Wage Estimates: Sector 62 - Health Care and Social Assistance," Bureau of Labor Statistics, 2017. [Online]. Available: https://www.bls.gov/oes/current/naics2_62.htm. [Accessed 14 August 2018].

[5] Eastern Research Group (ERG), "Economic Threshold and Regulatory Flexibility Assessment of Proposed Changes to the Current Good Manufacturing Practice Regulations for Manufacturing, Processing, Packing, or Holding Drugs," 1995.

[6] Bureau of Labor Statistics, "May 2017 National Industry-Specific Occupational Employment and Wage Estimates NAICS 325400 - Pharmaceutical and Medicine Manufacturing," Bureau of Labor Statistics, 2017. [Online]. Available: https://www.bls.gov/oes/current/naics4_325400.htm. [Accessed 14 August 2018].

[7] US Small Business Administration, "Table of Small Business Size Standards Matched to North American Industry Classification System Codes," US Small Business Administration, 2017.