DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Annual Summary Reporting Requirements Under the Right to Try Act

Docket No. FDA-2019-N-5553

Preliminary Regulatory Impact Analysis
Initial Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis

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I. Introduction and Summary

A. Introduction

We have examined the impacts of the proposed 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." This proposed 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 effects are low in cost and minimally dispersed, we propose to certify that the proposed 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 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 $154 million, using the most current

(2018) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Summary of Costs and Benefits

This proposed rule, if finalized, implements a statutory requirement in the Right to Try Act that sponsors and manufacturers who provide an eligible investigational drug under the Right to Try Act to eligible patients submit to the Food and Drug Administration (FDA) an annual summary of such use. The Right to Try Act requires FDA to specify by regulation the deadline, and requires that submissions include certain information.

The proposed rule's costs are summarized in Table 1; we are unable to quantify benefits for this rule. This analysis estimates the incremental impacts of this proposed rule, if finalized, for drug sponsors and these annual summary reports. Costs are calculated as the time spent by firms to prepare and submit annual summary reports based on participation in Right to Try Act requests from eligible patients for investigational new treatments. The total estimated present value of this rule's costs is $39,991 at a seven percent discount rate and $49,345 at a three percent discount rate (in 2018 dollars). The annualized cost of this rule over ten years is $5,694 at a seven percent discount rate and $5,785 at a three percent discount rate.

The benefits of this rule consist of societal and public health outcomes that may accrue from the disclosure of the use of investigational drugs and any known serious adverse events provided in these annual summary reports. Without these reports, FDA would not be made aware in a systematic manner of the use of eligible drugs under the

Right to Try Act and any known serious adverse events. With these reports, there may be increased awareness of investigational drugs, the diseases or conditions for which patients are seeking access, and any known serious adverse events associated with such use.

These reporting requirements instruct firms to collect all known serious adverse events and submit them once per year to the FDA. In addition, based on the information in these annual summaries, FDA intends to post an annual summary report in accordance with section 561B(d)(2) of the FD&C Act. FDA's posting of these reports may increase awareness about the availability of investigational drugs. In some cases, access to such drugs may help treat future patients.

Consistent with Executive Order 12866, Table 1 provides the costs and a description of benefits for this proposed rule over a ten year period.

Table 1: Summary of Benefits and Costs in 2018 Dollars Over a Ten-Year Time Horizon

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized $/year				2018	7%	10	
					2018	3%	10	
	Annualized Quantified					7%		
						3%		
	Qualitative							Disclosure of serious adverse events and outcomes related to investigational new drug treatments.
Costs	Annualized Monetized $/year	$5,694			2018	7%	10	
		$5,785			2018	3%	10	
	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 continuing over an infinite time horizon.

Table 2 – EO 13771 Summary Table (in 2016 dollars, over a perpetual time horizon)

	Primary (7%)	Primary (3%)
Present Value of Costs	$63,120	$176,799
Present Value of Cost Savings		
Present Value of Net Costs	$63,120	$176,799
Annualized Costs	$4,418	$5,304
Annualized Cost Savings		
Annualized Net Costs	$4,418	$5,304

II. Preliminary Economic Analysis of Impacts

A. Background

The Right to Try Act was signed into law in May 2018, creating section 561B of the Federal Food, Drug, and Cosmetic (FD&C) Act. This new law amends the FD&C Act to establish an option for patients who meet certain criteria to request access to certain

unapproved medical products, and for sponsors and manufacturers who agree to provide certain unapproved medical products other than through FDA's expanded access program. The law establishes a new pathway for patients to request, and manufacturers or sponsors to choose to provide, access to certain unapproved, investigational treatments for patients diagnosed with life-threatening diseases or conditions who have exhausted approved treatment options and who are unable to participate in a clinical trial involving the investigational drug. The Right to Try Act is designed to facilitate patients' access to certain investigational drugs from manufacturers and sponsors who may choose to provide such drugs – a process in which FDA is not involved.

Manufacturers or sponsors who provide their investigational drug under the Right to Try Act are required to submit to FDA an annual summary of drugs supplied to eligible patients. Specifically, this annual summary must include the name of the investigational drug, the number of doses supplied, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events. FDA is required to specify the deadline for such reporting submissions. This proposed rule, if finalized, will provide information on the necessary contents of the annual summary and the deadline for its submission.

B. The Need for Federal Regulatory Action

The Right to Try Act requires FDA to specify by regulation the deadline of submission of an annual summary of an eligible investigational drug supplied by manufacturers or sponsors to eligible patients. This proposed rule, if finalized, would implement this provision of the Right to Try Act. This regulation would allow, if

finalized, FDA to receive information about Right to Try Act access and activity, including any known serious adverse events. Requests for access under the Right to Try Act are not overseen by FDA. This rule would provide a mechanism for FDA to receive information about the use of drugs and adverse event data associated with the Right to Try Act in a systematic manner.

C. Purpose of the Proposed Rule

The purpose of this proposed rule is to implement section 561B(d)(1) of the FD&C Act, as amended by the Right to Try Act, which requires sponsors and manufacturers who provide an eligible investigational drug under section 561B of the FD&C Act to submit to FDA an annual summary of such use and requires FDA to specify by regulation the deadline of submission. The proposed rule, if finalized, would provide information on the necessary contents of the annual summary along with the deadline for its submission. Under this proposed rule, FDA would establish an email address or electronic portal for these submissions.

D. Baseline Conditions

This proposed rule is part of the implementation of the Right to Try Act, and so the baseline conditions refer to current conditions where the legislation has been enacted, but the rule not yet promulgated; thus, patients and physicians are currently able to determine eligibility, and drug sponsors are currently able to supply eligible investigational drugs under the Right to Try Act if they are willing to do so.

However, FDA has not yet specified by regulation the requirements for the content and the deadline for submission of an annual summary report. This regulation would affect any drug manufacturers or sponsors that provide an eligible investigational drug to eligible patients under the Right to Try Act. We assume these drug sponsors, when providing such eligible investigational new drugs to eligible patients, will have information on the number of doses that they supplied, the life-threatening disease for which the investigational drug was made available under the Right to Try Act, and known serious adverse events. The incremental burden drug sponsors may encounter from this regulation is the preparation and submission of the annual summary report described in the proposed rule based on information that was likely already collected.

E. Benefits of the Proposed Rule

The benefits of this rule consist of societal and public health outcomes that may accrue from the disclosure of the use of investigational drugs and any known serious adverse events provided in these annual summary reports. Without these reports, FDA would not be made aware in a systematic manner of the use of eligible drugs under the Right to Try Act and any known serious adverse events. With these reports, there may be increased awareness of investigational drugs, the diseases or conditions for which patients are seeking access, and any known serious adverse events associated with such use.

These reporting requirements instruct firms to collect all known serious adverse events and submit them once per year to the FDA. In addition, based on the information in these annual summaries, FDA intends to post online an annual summary report in

accordance with section 561B(d)(2) of the FD&C Act. FDA's posting of these reports may increase awareness about the availability of investigational drugs.

F. Costs of the Proposed Rule

This proposed rule implements a statutory requirement: the date of a submission of an annual summary report to be submitted by a drug manufacturer or sponsor providing an eligible investigational new drug to an eligible patient and includes the contents of the summary report. The incremental burden imposed by this proposed rule will be in the form of costs associated with the drug sponsors' compilation and submission of these summary reports. This proposed rule is related only to the submission of the annual summaries and not to the Right to Try Act requests made by patients. The provisions of this proposed rule are not necessarily expected to lead to additional Right to Try Act requests from patients. Thus, we do not expect that the proposed rule would lead to additional summaries and incremental cost burdens.

The Right to Try Act specifies the content of these annual summary reports. The drug sponsor's annual summary report would be required to include (1) the name of the investigational drug and applicable IND (investigational new drug) number, (2) number of doses supplied, (3) number of patients treated, (4) uses or conditions for which the drug was made available, and (5) any known serious adverse events or outcomes. The proposed rule includes an example of a tabular summary that could be used for these data fields and report submission to FDA.

The purpose and attributes, along with the intended preparer, of this annual summary report are close to the information required in Form FDA 2252. Form FDA

2252 is required to accompany all annual report submissions regarding new information that might affect the safety, effectiveness, or labeling of a drug or biological product for human use. The sponsor of the drug or biological product is responsible for collecting the relevant information and submitting this form to the FDA. The time required to complete this form has been previously estimated by the FDA to average five hours; this includes time to review instructions, search and gather the existing data, and complete the information collection[1]. Because the proposed rule's tabular summary requires fewer required data elements (such as Field 8: Reporting Period in Form FDA 2252) and less summary information overall, we halve this time estimate to 2.5 hours. We request comment and data on these assumptions and estimates.

We assume a medical director or regulatory affairs director will be responsible for preparing and submitting this annual summary report. The mean hourly wage (in 2018) for Medical and Health Services Managers in the Pharmaceutical and Medicine Manufacturing industry was $106.39 [Ref. 1]. The total cost of labor is the fully-loaded wage, which includes overhead and benefits. We assume that the cost of overhead and benefits equals 100% of the wage, resulting in a fully-loaded total hourly wage of $212.78. We estimate a cost of $531.95 (=$212.78 * 2.5 hours) to prepare and submit each report.

Between passage of the Right to Try Act in May 2018 and January 2019, there were two publicly reported instances of patients who have received access to

[1] This estimate for Form FDA 2252 has been reviewed and approved by the Office of Management and Budget. It was approved under OMB control number 0910–0001. See, Form FDA 2252 available at: https://www.fda.gov/media/73005/download; https://www.reginfo.gov/public/do/PRAViewDocument?ref_nbr=201704-0910-006.

investigational treatments via the Right to Try Act pathway, though it is possible that there are other cases that have not been made public[2]. The annual summary report must include data for the preceding calendar year. For manufacturers or sponsors that have supplied eligible investigational drugs between the period of enactment and the date the final rule becomes effective, the first annual summary would be submitted 60 days after the rule becomes effective and would include all uses of eligible investigational drugs May 30, 2018 through the effective date of the final rule. Based on the two instances publicly reported of so far, we estimate (and potentially overestimate) that there may be six summaries submitted by drug sponsors included in this initial group of reports. With increasing awareness of the Right to Try Act pathway for access to investigational drugs without being part of clinical trials, the number of individual patients seeking access to such treatments may rise. There is uncertainty concerning the extent of this increase, however. There may be some increase in the years following passage of the Right to Try Act, which may at some point level off or even decline. Table 3 outlines our assumptions and estimates for the expected number of Right to Try Act annual summary reports submitted. The cost to prepare and submit each report, estimated above at $531.95, is multiplied by the estimated number of annual reports we expect to receive over a ten-year period (six in year one, eight in year two, twelve in each subsequent year) to obtain the overall estimated costs of preparing and submitting these annual summary reports. We request comment on our assumptions and the number of years stakeholders expect the impacts of the proposed rule, if finalized, would continue.

[2] https://med.nyu.edu/pophealth/divisions/medical-ethics/compassionate-use#Q21

Table 3: Expected Increase and Estimated Number of Right to Try Act Annual Summary Reports

Year After Passage of Right to Try Act	Expected Percent Increase in Patient Requests and Annual Reports	Expected Number of Annual Reports
1	30	6
2	40	8
3	50	12
4	0	12
5 - 10	0	12

G. Distributional Effects

We do not expect there to be any distributional effects of this rule. This proposed rule outlines the contents and deadline for an annual summary report submitted to FDA by drug sponsors and is not expected to generate any disproportionate impact on any specific industry or population group.

H. International Effects

We do not expect there to be any significant international effects of this proposed rule. Both domestic and international drug sponsors would be subject to this annual summary reporting requirement.

III. Initial 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 number of annual summary reports is anticipated to be relatively small (as a percentage of all investigational new drugs) and widely dispersed, we propose to certify that the

proposed 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 Initial Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

The Small Business Administration defines an entity in the pharmaceutical industry as small if it has fewer than 1,250 employees. Based on this definition, about 90 percent of the drug entities are small. The impact on each entity will vary depending on its information collection capabilities when the rule is implemented, but all firms within this sector are familiar with the data and categories that comprise this annual summary report. The submission and data collection requirements are generally straight-forward and appropriate to the investigational new drug process. We request detailed comments and data on the number of small entities that would be affected by the proposed rule, as well as data on the economic impact of the proposed rule on these small entities.

IV. References

[1] U.S. Bureau of Labor Statistics, May 2018. National Occupational Employment and Wage Estimates United States. 2018. Available from: https://www.bls.gov/oes/2018/may/oes_nat.htm.