DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations

Docket No. FDA-2018-N-2727

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

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I. Economic Analysis of Impacts

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). We believe that this proposed rule is not a significant regulatory action as defined by Executive Order 12866. 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 the proposed rule is an Executive Order 13771 deregulatory action and does not require us to identify cost offsets.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule does not impose new requirements on any entity and therefore has no associated compliance costs, 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 $148 million, using the most current (2016) 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 Benefits, Cost Savings, and Costs

We do not anticipate additional costs associated with this rulemaking. This proposed rule would help enable the conduct of certain minimal risk clinical investigations for which the requirement to obtain informed consent is waived or for which certain elements of informed consent are waived or altered. We expect benefits in the form of healthcare advances from such minimal risk clinical investigations and from harmonization of FDA's informed consent regulations with the Common Rule's provision for waiver of informed consent for certain minimal risk research. We cannot quantify all of these benefits because of the lack of relevant data available to FDA. The benefits that we are able to quantify are the cost savings to IRBs because the time burdens of reviewing certain minimal risk clinical investigations under differing requirements would be reduced. The estimated cost savings of the proposed rule are approximately $237.6 thousand, with a lower bound of $59.4 thousand and an upper bound of $950.5 thousand. The estimated annualized costs savings of the proposed rule are approximately $27 thousand, with a lower bound of approximately $6,762 and an upper bound of approximately $108.2 thousand, discounted at 3 percent over 10 years. The estimated annualized costs savings of the proposed rule are approximately $26 thousand, with a lower bound of approximately $6,509 and an upper bound of $104.1 thousand, discounted at 7 percent over 10 years. The cost savings and costs of the proposed rule are summarized in table 1.

Table 1.—Summary of Cost Savings, Costs, and Distributional Effects of the Proposed Rule								
Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Cost Savings	One-time Monetized millions/year							
	Annualized Quantified	$26.0K	$6.5K	$104.1K	2016	7%	10 years	
		$27.0K	$6.8K	$108.2K	2016	3%	10 years	
	Qualitative							
Costs	Annualized							
	Monetized millions/year							
	Annualized							
	Quantified							
	Qualitative	$0			2016		10 years	
Transfers	Federal Annualized							
	Monetized $millions/year							
		From:			To:			
	Other Annualized							
	Monetized $millions/year							
		From:			To:			
Effects	State, Local or Tribal Government:							

C. Benefits of the Proposed Rule

The proposed rule would amend FDA's current informed consent regulations to harmonize with the 1991 version of the Common Rule's provision for waiver of the requirement to obtain informed consent for certain minimal risk research. We expect benefits in the form of healthcare advances stemming from additional minimal risk clinical investigations that would proceed using a waiver or alteration of informed consent, and from harmonization with the Common Rule's provision for waiver of the requirement to obtain informed consent for certain minimal risk research. The Common Rule provision is currently used by numerous other Federal departments and agencies. Some clinical research is subject to both FDA's regulations and the

Common Rule, so harmonization of this specific waiver provision would benefit those entities that conduct, sponsor, or review certain minimal risk clinical investigations by reducing confusion and burden created by the need to comply with differing requirements.

D. Cost Savings of the Proposed Rule

The proposed rule would harmonize FDA's informed consent regulations with the 1991 version of the Common Rule's provision for waiver of the requirement to obtain informed consent for certain minimal risk clinical investigations. As in a previous economic analysis of the 2017 revisions to the Common Rule (Ref. 1), we attempt to quantify the effects of the proposed rule where possible. We conducted a search for active IRBs regulated by both FDA and the Office for Human Research Protections (OHRP) in HHS in the "Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in the Last 60 Days" (Ref. 2). Using this data, we are able to determine whether an IRB is active or inactive, and whether it is regulated by FDA, OHRP, or both. We multiply the number of active IRBs by the percentage of IRBs regulated by both FDA and OHRP to yield an estimate of 2,442 active IRBs that are regulated by both FDA and OHRP (= 3,507 × 0.696). We expect that some of these IRBs would be affected by the proposed rule, and would experience a reduction in the time burden of determining whether to approve a waiver of the requirement to obtain informed consent for a minimal risk clinical investigation by reviewing it under a harmonized standard.[1] We estimate that 50 percent of affected IRBs would incur time savings from the proposed rule, with a lower bound of 25 percent of affected IRBs and an upper

[1] As previously discussed, the revised Common Rule adds a fifth criterion to the waiver or alteration of informed consent requirements (see section II.A). Although FDA is not proposing to adopt the fifth criterion in this rulemaking, for clinical investigations subject to both the Common Rule and FDA regulations, if an IRB finds and documents that research satisfies the criteria for waiver of the requirement to obtain informed consent for minimal risk research under the revised Common Rule, then that research would also meet the standards for waiver of the requirement to obtain informed consent in FDA-regulated clinical investigations described in this proposed rule.

bound of 100 percent of affected IRBs. We estimate that for affected IRBs, cost savings would be incurred in the form of time savings to IRB administrators, IRB chairs, IRB voting members, and IRB administrative staff from evaluating a minimal risk clinical investigation under FDA's and the Common Rule's harmonized regulations for waiving the requirement to obtain informed consent. Based on discussion with FDA subject matter experts (Ref. 3), we estimate that the reduced time burden of the proposed rule is 30 minutes (0.5 hours), with a lower bound of 15 minutes (0.25 hours) and an upper bound of 60 minutes (1 hour).

We draw from Bureau of Labor Statistics data to estimate hourly wage rates for IRB chairs, IRB voting members, and IRB administrative staff in 2016 dollars. Based on an economic analysis of impacts of revisions to the Common Rule (Ref. 1), we use wages for postsecondary education administrators to proxy for IRB administrator wages (Ref. 4), wages for office and administrative support workers to proxy for IRB administrative staff wages (Ref. 5), and wages for postsecondary health teachers to proxy for the wages of IRB chairs and IRB voting members (Ref. 6). We double each hourly wage to account for benefits and overhead, yielding wage rates of $134.50 for IRB administrators (= $67.25 × 2), $35.94 for IRB administrative staff (= $17.97 × 2), $109.40 for IRB chairs (= $54.70 × 2), and $109.40 for IRB voting members (= $54.70 × 2). We estimate that each of these forms of labor would experience time savings as a result of the proposed rule ranging from 15 to 60 minutes, with a central estimate of 30 minutes. We also estimate that time savings would be incurred by one IRB administrator, one IRB administrative staff, one IRB chair, and one IRB voting member. We multiply the number of active IRBs regulated by the percentage of IRBs affected by the proposed rule, the estimated reduced time burden of the proposed rule, and the sum of each IRB wage rate to yield a total estimated cost savings of approximately $237,631 (= 2,442 × 0.50 × 0.50 ×

[$134.50 + $109.40 + $109.40 + $35.94]), with lower bound estimated cost savings of approximately $59,408 (= 2,442 × 0.25 × 0.25 × [$134.50 + $109.40 + $109.40 + $35.94]) and upper bound estimated cost savings of approximately $950,524 (= 2,442 × 1 × 1 × [$134.50 + $109.40 + $109.40 + $35.94]). The net present value of the cost savings of the proposed rule is approximately $230.7 thousand, discounted at 3 percent, with a lower bound of approximately $57.7 thousand and an upper bound of approximately $922.8 thousand. The net present value of the cost savings of the proposed rule are approximately $222.1 thousand, discounted at 7 percent, with a lower bound of approximately $55.5 thousand and an upper bound of approximately $888.3 thousand. The annualized cost savings of the proposed rule are approximately $27 thousand, discounted at 3 percent over 10 years, with a lower bound of approximately $6,762 and an upper bound of approximately $108.2 thousand. The annualized cost savings of the proposed rule are approximately $26 thousand discounted at 7 percent over 10 years, with a lower bound of approximately $6,509 and an upper bound of approximately $104.1 thousand. The estimated cost savings of the proposed rule to IRBs are summarized in table 2.

Table 2.--Cost Savings of the Proposed Rule to IRBs

	Low	Middle	High
No. of active IRBs	3,507	3,507	3,507
Percentage of IRBs regulated by FDA and OHRP	69.6%	69.6%	69.6%
No. of active IRBs regulated by FDA and OHRP	2,442	2,442	2,442
Percentage of FDA/OHRP regulated IRBs affected by the proposed rule	25%	50%	100%
Reduced time burden of the proposed rule (hours)	0.25	0.5	1
Hourly wage, IRB administrator	$134.50	$134.50	$134.50
Hourly wage, IRB chair	$109.40	$109.40	$109.40
Hourly wage, IRB voting member	$109.40	$109.40	$109.40
Hourly wage, IRB administrative staff	$35.94	$35.94	$35.94
Total cost savings of the proposed rule	$59,408	$237,631	$950,524
Net present value of the proposed rule (3%)	$57,677	$230,710	$922,839
Net present value of the proposed rule (7%)	$55,521	$222,085	$888,340
Annualized cost savings of the proposed rule (3%, 10 years)	$6,762	$27,046	$108,185
Annualized cost savings of the proposed rule (7%, 10 years)	$6,509	$26,035	$104,141

E. Costs of the Proposed Rule

We do not anticipate additional costs associated with this rulemaking. This proposed rule would help enable the conduct of certain minimal risk clinical investigations for which the requirement to obtain informed consent is waived or for which certain elements of informed consent are waived or altered.

F. Executive Order 13771

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 the proposed rule, if finalized, is deregulatory under Executive Order 13771 and does not require us to identify cost offsets.

The net present value of the cost savings of the proposed rule are approximately $222.1 thousand, discounted at 7 percent, with a lower bound of approximately $55.5 thousand and an upper bound of approximately $888.3 thousand. The annualized cost savings of the proposed rule are approximately $15,546, discounted at 7 percent on an infinite time horizon, with a lower bound of approximately $3,886 and an upper bound of approximately $62,184. Discounted at 3 percent, the net present value of the cost savings of the proposed rule are approximately $230.7 thousand, with a lower bound of approximately $57.7 thousand and an upper bound of approximately $922.8 thousand. The annualized cost savings of the proposed rule are approximately $6,921, discounted at 3 percent on an infinite time horizon, with a lower bound of approximately $1,730 and an upper bound of approximately $27,685. The estimated net cost savings under Executive Order 13771 are summarized in table 3.

Table 3.--Summary of Executive Order 13771 Net Cost Savings

	Primary (7%)	Lower Bound (7%)	Upper Bound (7%)	Primary (3%)	Lower Bound (3%)	Upper Bound (3%)
Present Value of Costs	-	-	-	-	-	-

Present Value of Cost Savings	$222,085	$55,521	$888,340	$230,710	$57,677	$922,839
Present Value of Net Cost Savings	$222,085	$55,521	$888,340	$230,710	$57,677	$922,839
Annualized Costs	-	-	-	-	-	-
Annualized Cost Savings	$15,546	$3,886	$62,184	$6,921	$1,730	$27,685
Annualized Net Cost Savings	$15,546	$3,886	$62,184	$6,921	$1,730	$27,685

II. References

The following references are on display in the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at https://www.regulations.gov. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. Government Publishing Office, "Federal Policy for the Protection of Human Subjects", 82 FR 7149 (January 19, 2017), available at: https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf, accessed on September 20, 2017.

2. Memorandum to File, FDA summary of data analysis; HHS, "Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in Last 60 Days", prepared by Christian Brown, FDA, September 20, 2017.

3. Memorandum to File, FDA staff meeting on the Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations rulemaking, prepared by Christian Brown, FDA, September 20, 2017, addendum August 20, 2018.

4. Bureau of Labor and Statistics, “Occupational Employment and Wages, May 2016, 11-9033 Education Administrators, Postsecondary”, available at: https://www.bls.gov/oes/2016/may/oes119033.htm, accessed on September 20, 2017.

5. Bureau of Labor and Statistics, “Occupational Employment and Wages, May 2016, 43-0000 Office and Administrative Support Occupations (Major Group)”, available at: https://www.bls.gov/oes/2016/may/oes430000.htm, accessed on September 20, 2017.

6. Bureau of Labor and Statistics, “May 2016 National Occupational Employment and Wage Estimates, United States”, available at: https://www.bls.gov/oes/2016/may/oes_nat.htm, accessed on September 20, 2017.