DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products;

Final Rule

Docket No. FDA- 2000-N-0009

(formerly Docket No. 2000-N-0074)

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

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I. Analysis of Impacts

A. Introduction

FDA has examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct Agencies 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). The Agency believes that this final rule is not a significant regulatory action under Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. The Agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies 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 $139 million, using the most current (2011) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

B. Updated Analysis

The interim final rule (66 FR 20589 at 20596, April 24, 2001) imposed an additional burden on IRBs reviewing investigations which involve children. The estimated costs of the interim final rule were estimated to be small ($933,000 in year 2001 and $23,550 per year in years 2002 through 2009). As the interim final rule has been in effect since April 2001, the publication of this final rule will have little additional impact. However, we update the estimated costs of the interim rule for the post-2001 period to adjust for inflation and availability of more recent data. The total annual cost of reviewing pediatric clinical trials remains at $933,000 (this includes a one-time cost of $900,000 to conduct a one-time review and update standard operating procedures plus $33,000 for annual reviews) for the year 2001. The revised annual review cost for the post-2001 period ranges between $79,817 and $112,357 per year (see table 1 in this document).

The revised post-2001 costs per year are revised as follows. First, the annual IRB costs per year are in inflation-adjusted (2010) dollars. Second, we use recent data from the various FDA centers reviewing protocols involving pediatrics, and update the total number of studies affected by the rule to be between 872 and 1,227 per year. We note that given data limitations we are unable to use the same period of analysis across centers. To the extent that there has been an increase in the number of protocols involving children since 2001, then using the most recently available data would provide an upper bound estimate on the average number of protocols received after 2001. However, over the past few years, most offices within FDA's Center for Drug Evaluation and Research (CDER) did not observe a significant increase in the percentage change of protocols received. Thus, we believe that the impact of using different periods of data

is negligible. The data and methodology used are discussed in more detail in the paragraphs that follow.

The estimated number of drug- and biologics-related protocols involving pediatrics ranges from 561 to 637. The number of drug-related or biologics-related protocols (553 to 610) provided by CDER was based on data from fiscal year 2011. The range of protocols related to biological products regulated by FDA's Center for Biologics Evaluation and Research (CBER) represents the minimum (8 in fiscal year 2004) and maximum (27 in fiscal year 2011) number of pediatric protocols received by CBER during fiscal years 2002-2011. The count is adjusted up 30 percent[1] to account for IND-exempt protocols.

We estimate that 305 to 572 medical device protocols involve pediatrics. This is calculated by using the average number of applications or submissions (including supplements) reviewed by FDA's Center for Devices and Radiological Health per year and an estimate on the percent of medical device applications involving children. We estimate that, using the number of approved IDE pediatric studies as reported by FDA's Center Tracking System (7 to 13), and the average number of original IDE submissions (219) in fiscal years 2008-2009, 3 percent to 6 percent of medical device protocols involve pediatrics. We note that there could be some high-risk medical devices which might not be included in our estimated number of protocols for medical devices; however, data limitations do not permit us to quantify the extent to which our estimates would have to be adjusted up.

Finally, the estimated number of protocols for food additives and infant formula are extrapolated using the average High-to-Low ratio (3-to-1) across the other products and the

[1] This estimate is determined based on discussions with academic and commercial IRBs on the estimated percent of pediatric protocols which are exempt from filing an IND application.

initial estimates in the final rule. For instance, to determine the upper-bound estimate for infant formula we multiply the 2001 estimate by the High-to-Low ratio (5 x 3).

Table 1.--Estimated Number of IRB Reviews per year for Clinical Investigations in Children			
		Per year post-2001	
	2001	Low	High
Drugs and Biological Products	264	561	637
Medical Devices	170	305	572
Foods and Food Additives			
Infant Formula	5	5	15
Food Additives	1	1	3
Total IRB Reviews per year	440	872	1,227
Total IRB Costs per year	$33,000	$79,817	$112,357