DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Labeling Requirements for Approved and Conditionally Approved New Animal Drugs; Proposed Rule

Docket No. FDA-2023-N-5160

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

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Executive Summary

If this proposed rule is finalized, industry and FDA would incur cost savings from a reduction in the quantity and time burden of new animal drug labeling amendments and informal communications related to new animal drug labeling. There may be additional benefits to users of approved or conditionally approved new animal drugs from greater predictability and ease of reading new animal drug labeling in the form of time saved searching for content, as well as benefits to animal or human health, which we are unable to quantify.

We expect that new animal drug sponsors would incur one-time costs to read and understand the rule, revise standard operating procedures (SOPs) related to labeling, and train employees on the revised SOPs. New animal drug sponsors would also bear costs to update labeling and prepare supplemental labeling applications to conform to the proposed requirements. FDA would incur costs to review these supplemental applications.

FDA estimates that the annualized benefits over 10 years would range from $0.143 million to $0.243 million at a 2 percent discount rate, with a primary estimate of $0.193 million. The annualized costs would range from $2.16 million to $2.77 million at a 2 percent discount rate, with a primary estimate of $2.45 million.

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A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 14094, 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, 13563, and 14094 direct us to assess all benefits, costs, and transfers 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). Rules are "significant" under Executive Order 12866 Section 3(f)(1) (as amended by Executive Order 14094) if they "have an annual effect on the economy of $200 million or more (adjusted every 3 years by the Administrator of [the Office of Information and Regulatory Affairs (OIRA)] for changes in gross domestic product); or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, territorial, or tribal governments or communities." OIRA has determined that this proposed rule is not a significant regulatory action as defined by Executive Order 12866 Section 3(f)(1).

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because net annualized compliance costs of the proposed rule are less than 2 percent of average annual revenues for the smallest firms in the industry, 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 impacts, 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 $177 million, using the most current (2022) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in expenditure in any year that meets or exceeds this amount.

B. Overview of Costs and Benefits

The proposed rule, if finalized, would require that sponsors follow specific content and format requirements for labeling of approved or conditionally approved new animal drugs. A comprehensive set of standardized requirements for the content and format of information on labeling of such drugs currently does not exist. Veterinarians, pet owners, livestock owners, and other users of new animal drugs may more easily locate the information they need with standardized labeling.

We quantify potential cost savings to industry and FDA from a reduction in the quantity and time burden of new animal drug labeling amendments and informal communications related to new animal drug labeling. There may be additional benefits to users of approved or conditionally approved new animal drugs from greater predictability and ease of reading new animal drug labeling in the form of time saved searching for content. We are unable to quantify these potential benefits to users, but we perform a breakeven analysis to estimate how large these non-quantified benefits would have to be to bridge the gap between quantified benefits and costs. Our breakeven analysis suggests that the primary estimate of the annualized costs over 10 years at a 2 percent discount rate would equal the annualized benefits if each veterinarian in the United States saved an average of 9 minutes per year, if each pet owner saved an average of 3 seconds per year, or if each livestock owner saved an average of 1 minute per year on these tasks. We present this breakeven analysis in Section II.G. Animal or human health benefits additionally may result from reductions in medication errors or improvements in adverse event reporting, which we cannot quantify.

We expect that new animal drug sponsors would incur one-time costs to read and understand the rule, revise standard operating procedures (SOPs) related to labeling, and train employees on the revised SOPs. New animal drug sponsors would also bear costs to update labeling and prepare supplemental labeling applications to conform to the proposed requirements. FDA would incur costs to review these supplemental applications.

We summarize the quantified benefits and costs in Table 1. We estimate that the annualized benefits over 10 years would range from $0.143 million to $0.243 million at a 2 percent discount rate, with a primary estimate of $0.193 million. The annualized costs would range from $2.16 million to $2.77 million at a 2 percent discount rate, with a primary estimate of $2.45 million.

The present value of total benefits over 10 years would range from $1.31 million to $2.23 million at a 2 percent discount rate, with a primary estimate of $1.77 million. At a 2 percent discount rate, the present value of total costs would range from $19.78 million to $25.38 million, with a primary estimate of $22.48 million.

Table 1. Summary of Benefits, Costs, and Distributional Effects of the Proposed Rule (millions of 2022 dollars)

Category	*Primary Estimate*	*Low Estimate*	*High Estimate*	*Dollar Year*	*Discount Rate*	*Time Horizon*	*Notes (e.g., Risk Assumptions; Source Citations; Whether Inclusion of Capital Effects Differs Across Low, Primary, High Estimates; etc.)*
BENEFITS							
Annualized monetized benefits	$0.193	$0.143	$0.243	2022	2%	10 years	Cost savings to industry and FDA
Annualized quantified, but non-monetized, benefits							
Unquantified benefits	Information search cost savings to users of new animal drugs and potential benefits to animal or human health						
COSTS							
Annualized monetized costs	$2.45	$2.16	$2.77	2022	2%	10 years	
Annualized quantified, but non-monetized, costs							
Unquantified costs							
TRANSFERS							
Annualized monetized Federal budgetary transfers							
Bearers of transfer gain and loss?							
Other annualized monetized transfers							
Bearers of transfer gain and loss?							
NET BENEFITS							
Annualized monetized net benefits	−$2.26	−$2.02	−$2.53	2022	2%	10 years	

Category	*Effects*	*Notes*
Effects on State, local, or Tribal governments	None	
Effects on small businesses	Quantified effects of less than 2 percent of average annual revenues for the smallest firms	
Effects on wages	None	
Effects on growth	None	

II. Preliminary Regulatory Impact Analysis

A. Background

The proposed rule, if finalized, would revise the existing requirements for the content and format of labeling for approved or conditionally approved new animal drugs that sponsors submit as part of new animal drug applications (NADAs) or conditionally approved new animal drug applications (CNADAs), respectively. The proposed rule would also place labeling requirements that are specific to approved or conditionally approved new animal drugs in a single location in the Code of Federal Regulations (CFR). The proposed rule would apply to the labeling of both prescription (Rx) and over-the-counter (OTC) new animal drugs, as well as new animal drugs for use in animal feeds. We base the proposed requirements on FDA's long-standing practices and current thinking for reviewing labeling in new animal drug applications.

B. Potential Need for Federal Regulatory Action

Inadequate information on labeling represents a market failure. Users of new animal drugs, including veterinarians and animal owners, may not make optimal consumption decisions when they find it costly or time-consuming to locate information on product labeling. This may result in a less than optimal demand for the product. Uniform labeling across new animal drugs would result in lower information search costs for users of new animal drugs.

Additionally, new animal drug sponsors currently cannot consult all labeling regulations in a central location in the CFR. Some existing labeling regulations also refer to the use of labeling statements that are out-of-date or no longer consistent with our current position regarding the information that is necessary for the safe and effective use of new animal drugs. This has resulted in inefficiencies in the development and pre-market review of new animal drug applications. The proposed rule, if finalized, would reduce these inefficiencies by establishing standardized requirements for the content and format of new animal drug labeling and by placing labeling requirements in a single location in the CFR.

C. Purpose of the Proposed Rule

A comprehensive set of regulations establishing requirements for the labeling of new animal drugs currently does not exist. The proposed regulations, if finalized, would revise existing requirements for the labeling of approved or conditionally approved new animal drugs to ensure their safe and effective use. Also, these regulations would help sponsors more efficiently prepare labeling for approved or conditionally new animal drugs by providing clear and consistent requirements for the content and format of each labeling component.

In this document, we use the term "effective date" to refer to the date of finalization of the proposed rule.

The proposed rule, if finalized, would identify the specific labeling components that are required and permitted for each approved or conditionally approved new animal drug, including

the package insert, immediate container label, secondary container labeling, shipping labeling, and other labeling components, such as display cartons and multi-unit carton labeling. The proposed rule, if finalized, would also identify the information needed for each component, and the order in which information would appear.

The proposed rule, if finalized, would require sponsors of approved or conditionally approved new animal drugs to comply with these requirements according to the compliance schedule in the proposed rule. We base the compliance schedule on NADA number, beginning with the most recently approved applications. The schedule extends 6 years from the effective date of the final rule. We would require new animal drug sponsors to submit one supplemental application (supplement) with conforming labeling for each previously approved NADA.

We would not require the labeling for new animal drugs that we conditionally approve before the effective date of the final rule to comply during the conditional approval period (unless the sponsor submits a supplement subject to 21 CFR part 514.8(c)(2) to the CNADA after the effective date). Instead, sponsors of conditionally approved new animal drugs would need to comply with the proposed labeling requirements at the time they submit an application for full approval. We would require CNADAs that sponsors submit after the effective date of the final rule to comply in the initial CNADA.

We would not require NADAs or CNADAs that are pending Center for Veterinary Medicine (CVM) review on the effective date of the final rule or that we receive during the first 180 days after the effective date to conform to the new labeling requirements.[1] These sponsors would have the option to include the conforming labeling in (1) the initial application, (2) an amendment to the pending application, or (3) a supplement to the application after we approve it. The proposed rule, if finalized, would require these sponsors to submit labeling that conforms to the new labeling requirements within 180 days of the date on which we approve the application.

We assume that the number of labeling changes resulting from the proposed rule, if finalized, would exceed the number of new animal drug applications because new animal drug sponsors generally include multiple labeling components per application. In addition, we assume that a small number of new animal drug applications would include labeling that falls into more than one product type, specifically applications for new animal drugs that we have approved for both Rx and OTC use.

D. Baseline Conditions

1. Number of affected entities

The proposed rule, if finalized, would affect all sponsors of approved or conditionally approved new animal drug applications. Based on internal data from CVM, there were 78 unique firms with an approved or conditionally approved new animal drug application (sponsors) in

[1] This includes supplements subject to 21 CFR part 514.8(c)(2).

September 2023.[2] Sixty-six of these sponsors (85 percent) currently had an approved and marketed new animal drug.[3]

Based on the North American Industry Classification System (NAICS), the U.S. Census Bureau designates animal drug manufacturers as "pharmaceutical preparation manufacturers" (NAICS 325412). We use detailed firm size information from the U.S. Census Bureau's 2017 Statistics of U.S. Businesses (SUSB) to estimate the percentage of these firms that belong to different employment size categories (Ref. [1]).[4] We summarize these assumptions in Table 2.

Table 2. Affected Firms by Size Category

Employment size category	Percentage in size category[a]	Sponsors of approved drugs[b]	Sponsors of approved and marketed drugs[b]
0 to 4	33%	26	22
5 to 9	14%	11	9
10 to 19	11%	9	7
20 to 99	19%	15	13
100 to 499	12%	9	8
500 to 999	3%	2	2
1,000 to 1,499	1%	1	1
1,500+	7%	6	5
Total	100%	78	66

[a] We estimate the percentage in each size category based on SUSB data for NAICS 325412.
[b] Numbers do not sum to total due to rounding.

2. Number of affected applications

The proposed rule, if finalized, would establish the schedule for when sponsors of approved new animal drugs must conform to the labeling requirements using application numbers. The schedule would require more recently approved new animal drugs to conform to the requirements first since they are more likely to be consistent with the new requirements than the labeling of older new animal drugs. Sponsors of older new animal drug applications would have a longer amount of time to comply with the new requirements. The application numbers proposed as breakpoints would result in the submission of a similar number of labeling supplements during each one-year interval, based on the number of applications of approved and marketed new animal drugs as of September 1, 2023.

[2] In this estimate, we include sponsors of approved NADAs, approved abbreviated new animal drug applications (ANADAs), and CNADAs.
[3] For the purposes of this PRIA, an "approved and marketed new animal drug" is a new animal drug that (1) is the subject of an approved or conditionally approved new animal drug application, and (2) was marketed by the new animal drug sponsor in September 2023. We include conditionally approved new animal drugs in this definition because we assume that the 7 conditionally approved new animal drugs as of September 2023 will be subject to full approval by the effective date of the final rule. However, we note that not all conditionally approved new animal drugs will obtain full approval and, as we state in Section II.C, we would not require the labeling for new animal drugs that we conditionally approve before the effective date of the final rule to comply during the conditional approval period (unless the sponsor submits a supplement subject to 21 CFR part 514.8(c)(2) to the CNADA after the effective date).
[4] This is the most recent year for which detailed receipts information is available.

In accordance with the Generic Animal Drug and Patent Term Restoration Act of 1988 (GADPTRA), we expect that sponsors of approved abbreviated new animal drug applications (ANADAs) would also conform to the requirements when the reference-listed new animal drug conforms to the requirements. Therefore, we have also estimated the number of ANADAs that we expect to conform in each compliance period. We would require the labeling for ANADAs that reference a withdrawn NADA to conform during the first compliance period.[5] There are currently fewer than 10 such ANADAs.

Table 3 summarizes our assumptions regarding the number of applications that would be subject to each compliance period. We include only applications of approved and marketed new animal drugs in the group of affected applications, because we assume that sponsors will not incur labeling change costs for approved new animal drugs that they are not currently marketing. If sponsors choose to update labeling for approved new animal drugs that they are not currently marketing, we may underestimate these costs. We request comment on these assumptions.

Table 3. Number of Affected Applications in Each Compliance Period by NADA Number

NADA number	Compliance period[a]	Count of NADAs	Count of ANADAs with an RLNAD[b]	Total applications
N-141-300 +; certain ANADAs	1–2 years	104[c]	9	113
N-141-000 to N-141-299	2–3 years	101	86	187
N-115-000 to N-140-999	3–4 years	105	87	192
N-045-000 to N-114-999	4–5 years	116	68	184
N-000-001 to N-044-999	5–6 years	86	66	152
Total	All	512	316	828

[a] Time since publication of the final rule
[b] These are ANADAs that reference NADAs that have not been withdrawn (reference-listed new animal drugs [RLNADs]). We base the compliance period for each ANADA on the NADA number for the RLAND.
[c] This includes 6 ANADAs that reference a withdrawn NADA (5 Rx drugs and 1 OTC drug).

CVM has provided estimates for the number of affected NADAs by product type: Rx new animal drugs, OTC new animal drugs, Type A medicated articles,[6] combination medicated feeds, and proprietary Type B[7] and Type C[8] medicated feeds. Combination medicated feeds applications are separate applications that allow manufacturers to combine 2 or more previously approved Type A medicated articles into medicated feeds.

We present the distribution of the applications from Table 3 by product type in Table 4. We use these application counts to estimate the number of supplements that we expect new

[5] Specifically, these are reference-listed NADAs that have been voluntarily withdrawn for reasons other than safety or effectiveness, or that reference a new animal drug for which the NADA has been withdrawn on the basis of one or more of the grounds included under section 512(e) of FD&C Act and for which the ANADA's approval was not affected by the withdrawal.
[6] We define a Type A medicated article as a concentrated form of a drug for use in the manufacture of another Type A medicated article or medicated feeds (Type B or Type C).
[7] We define a Type B medicated feed by its use in the manufacture of other medicated feeds (Type B or Type C). A Type B medicated feed results from the dilution of a Type A medicated article or another Type B medicated feed with non-medicated feed, and at least 25 percent of its weight is from nutritional ingredients.
[8] Animals can directly consume Type C medicated feeds. A Type C medicated feed results from the dilution of a Type A medicated article, a Type B medicated feed, or another Type C medicated feed with non-medicated feed, and it contains a substantial quantity of nutritional ingredients.

animal drug sponsors would submit in each compliance period to comply with the proposed rule, if finalized. In our analysis, we assume that new animal drug sponsors would submit conforming labeling and incur associated costs at the beginning of each compliance period.

Table 4. Count of Affected Applications by Product Type for Each Compliance Period

Product type	Compliance period	Count of NADAs	Count of ANADAs	Total applications
Rx	Year 1–2	91	9	100
	Year 2–3	70	72	142
	Year 3–4	38	45	83
	Year 4–5	38	47	85
	Year 5–6	26	22	48
	Subtotal	263	195	458
OTC	Year 1–2	8	0	8
	Year 2–3	20	7	27
	Year 3–4	22	22	44
	Year 4–5	4	7	11
	Year 5–6	6	4	10
	Subtotal	60	40	100
Rx/OTC	Year 1–2	0	0	0
	Year 2–3	1	0	1
	Year 3–4	2	0	2
	Year 4–5	1	1	2
	Year 5–6	0	0	0
	Subtotal	4	1	5
Type A medicated articles	Year 1–2	5	0	5
	Year 2–3	6	4	10
	Year 3–4	14	3	17
	Year 4–5	12	1	13
	Year 5–6	19	5	24
	Subtotal	56	13	69
Combination medicated feeds	Year 1–2	0	0	0
	Year 2–3	1	3	4
	Year 3–4	21	17	38
	Year 4–5	42	12	54
	Year 5–6	34	35	69
	Subtotal	98	67	165
Proprietary Type B medicated feeds[a]	Year 1–2	0	0	0
	Year 2–3	0	0	0
	Year 3–4	1	0	1
	Year 4–5	1	0	1
	Year 5–6	0	0	0
	Subtotal	2	0	2
Proprietary Type C medicated feeds[a]	Year 1–2	0	0	0
	Year 2–3	3	0	3
	Year 3–4	7	0	7
	Year 4–5	18	0	18
	Year 5–6	1	0	1
	Subtotal	29	0	29

Product type	Compliance period	Count of NADAs	Count of ANADAs	Total applications
Total	Year 1–2	104	9	113
	Year 2–3	101	86	187
	Year 3–4	105	87	192
	Year 4–5	116	68	184
	Year 5–6	86	66	152
	Subtotal	512	316	828

[a] For some proprietary medicated feeds, we approve the formulation and labeling as part of an NADA. In other situations, a new animal drug sponsor maintains the underlying data and labeling for a proprietary Type B or Type C medicated feed in a Veterinary Master File (VMF). We account for both sources of labeling when calculating the number of affected NADAs that include proprietary Type B and Type C labeling in this table.

3. Number of affected labeling components and labeling packages

Each application may contain several labeling components that the proposed rule, if finalized, would affect. These may include the immediate container label, package insert, secondary container labeling, shipping labeling, and labeling associated with Type A medicated articles, and Type B and Type C medicated feeds. The number of labeling components per application can vary widely, depending on, for example, how new animal drug sponsors package a product, the number of sizes of immediate containers that sponsors market, and the variety of animals for which we approve the use of a Type A medicated article.

We summarize CVM estimates of the average number of labeling components per application for each product type in Table 5. We address shipping labeling separately in Section II.E.2.d.

Table 5. Average Number of Labeling Components per Application by Product Type

Product type	Labeling components per application	Notes
Rx	6	Immediate container (Rx label), package insert, and secondary container labeling for each of 2 sizes of an immediate container
OTC	6	Immediate container (OTC label), package insert, and secondary container labeling for each of 2 sizes of an immediate container
Type A medicated articles	6	1 proprietary Type A medicated article label and 5 components of representative labeling, or "Blue Bird" labeling, for medicated feeds that feed mills may manufacture from the Type A medicated article
Combination medicated feeds	5	All Blue Bird labeling for Type B and Type C medicated feeds
Proprietary Type B medicated feeds	2	1 proprietary Type B medicated feed label and 1 component of Blue Bird labeling for Type C medicated feeds that feed mills may manufacture from the proprietary Type B medicated feed
Proprietary Type C medicated feeds	3	All proprietary Type C medicated feed labels

A small number of applications, which we refer to as "Rx/OTC" applications, include more than one new animal drug, with at least one drug sold through prescription and at least one drug sold over-the-counter. Therefore, Rx/OTC applications involve both Rx and OTC labeling. To estimate the number of labeling components for these applications, we count these applications as both Rx applications and OTC applications.

In Table 6, we present our assumptions regarding the number of "proprietary" labeling components per application. These encompass all labeling components for Rx and OTC applications, the Type A medicated article label for Type A medicated article applications, the proprietary Type B medicated feed label for proprietary Type B medicated feed applications, and the proprietary Type C medicated feed labels for proprietary Type C medicated feed applications. Proprietary labeling components contain a mix of packaging materials, are professionally designed and printed, and often contain color (with the possible exception of the package insert).

The term "labeling package" refers to a unique presentation of the new animal drug that is approved or conditionally approved in an NADA or CNADA, respectively. There may be multiple unique presentations of the new animal drug that we approve or conditionally approve in the same application. Such presentations can vary by container size (e.g., the number of tablets in an immediate container), drug strength, or other distinctions, and each presentation may include some or all labeling components that are unique from other presentations (e.g., a unique label and secondary container labeling for each size of the immediate container).

We use CVM estimates of the average number of labeling packages per application by product type to estimate the number of affected labeling packages by application type and compliance period. We present these estimates in Table 6. Later in this analysis, we multiply these estimates by per package labeling cost estimates for human drugs to estimate proprietary labeling change costs.

Table 6. Number of Proprietary Labeling Components and Labeling Packages per Application

Product type	Average number of proprietary labeling components per application[a]	Average number of labeling packages per application
Rx	6	2
OTC	6	2
Rx/OTC	12	4
Type A medicated articles	1	1
Proprietary Type B medicated feeds	1	1
Proprietary Type C medicated feeds	3	3

[a] Excludes shipping labeling

In Table 7, we display our assumptions regarding the number of affected labeling packages by application type and compliance period for proprietary labeling components.

Table 7. Number of Affected Labeling Packages by Application Type and Compliance Period for Proprietary Labeling Components

Product type	Compliance period	Count of NADAs	Count of ANADAs	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total number of labeling package changes
Rx	Year 1–2	91	9	182	18	200
	Year 2–3	70	72	140	144	284
	Year 3–4	38	45	76	90	166
	Year 4–5	38	47	76	94	170
	Year 5–6	26	22	52	44	96
	Subtotal	263	195	526	390	916
OTC	Year 1–2	8	0	16	0	16
	Year 2–3	20	7	40	14	54
	Year 3–4	22	22	44	44	88
	Year 4–5	4	7	8	14	22
	Year 5–6	6	4	12	8	20
	Subtotal	60	40	120	80	200
Rx/OTC	Year 1–2	0	0	0	0	0
	Year 2–3	1	0	4	0	4
	Year 3–4	2	0	8	0	8
	Year 4–5	1	1	4	4	8
	Year 5–6	0	0	0	0	0
	Subtotal	4	1	16	4	20
Type A medicated articles	Year 1–2	5	0	5	0	5
	Year 2–3	6	4	6	4	10
	Year 3–4	14	3	14	3	17
	Year 4–5	12	1	12	1	13
	Year 5–6	19	5	19	5	24
	Subtotal	56	13	56	13	69
Proprietary Type B medicated feeds	Year 1–2	0	0	0	0	0
	Year 2–3	0	0	0	0	0
	Year 3–4	1	0	1	0	1
	Year 4–5	1	0	1	0	1
	Year 5–6	0	0	0	0	0
	Subtotal	2	0	2	0	2

Product type	Compliance period	Count of NADAs	Count of ANADAs	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total number of labeling package changes
Proprietary Type C medicated feeds	Year 1–2	0	0	0	0	0
	Year 2–3	3	0	9	0	9
	Year 3–4	7	0	21	0	21
	Year 4–5	18	0	54	0	54
	Year 5–6	1	0	3	0	3
	Subtotal	29	0	87	0	87
Total	Year 1–2	104	9	203	18	221
	Year 2–3	100	83	199	162	361
	Year 3–4	84	70	164	137	301
	Year 4–5	74	56	155	113	268
	Year 5–6	52	31	86	57	143
	Subtotal	414	249	807	487	1,294

In Table 8, we display the number of representative, i.e., "Blue Bird," labeling components per applicable application. Proprietary labels often provide "trade dress" information and artwork, are in color, and typically require professional printing. Blue Bird labeling, however, does not require professional printing. The typical Blue Bird labeling component is a simple document that includes a template containing only black and white text. Sponsors of new animal drugs create Blue Bird labeling for subsequent use by feed mills for the labeling of medicated animal feeds. Feed mills can easily modify the text-only Blue Bird labeling to make proprietary labeling that includes all pertinent "trade dress" information, artwork, and color for their medicated animal feed products. Labeling for approved medicated feed products does not include package inserts, secondary container labeling, shipping labeling, or any proprietary medicated feed labeling.

We present the counts for proprietary labeling and Blue Bird labeling separately because we estimate their costs of development and printing differently (see Table 8). In these calculations, we assume that, on average, each Type A medicated article application and each combination medicated feeds application, respectively, contains 5 Blue Bird labeling components and each Proprietary Type B medicated feed application contains 1 Blue Bird labeling component.

Table 8. Number of Affected Blue Bird Labeling Components by Application Type and Compliance Period

Product type	Compliance period	Count of NADAs	Count of ANADAs	Total number of Blue Bird labeling components
Type A medicated articles	Year 1–2	5	0	25
	Year 2–3	6	4	50
	Year 3–4	14	3	85
	Year 4–5	12	1	65
	Year 5–6	19	5	120
	Subtotal	56	13	345
	Year 1–2	0	0	0

Product type	Compliance period	Count of NADAs	Count of ANADAs	Total number of Blue Bird labeling components
Combination medicated feeds	Year 2–3	1	3	20
	Year 3–4	21	17	190
	Year 4–5	42	12	270
	Year 5–6	34	35	345
	Subtotal	98	67	825
Proprietary Type B medicated feeds	Year 1–2	0	0	0
	Year 2–3	0	0	0
	Year 3–4	1	0	1
	Year 4–5	1	0	1
	Year 5–6	0	0	0
	Subtotal	2	0	2
Total	Year 1–2	5	0	25
	Year 2–3	7	7	70
	Year 3–4	36	20	276
	Year 4–5	55	13	336
	Year 5–6	53	40	465
	Subtotal	156	80	1,172

E. Costs of the Proposed Rule

1. Administrative costs

In this section, we estimate one-time costs to industry for reading and understanding the rule; establishing, revising, and reviewing labeling SOPs; and training employees on changes to labeling SOPs. We assume that industry would bear these costs in year 0.

a. Reading and understanding the rule

All entities affected by the proposed rule, if finalized, would incur a one-time cost to read and understand this rule. We use the time required to complete this activity to estimate the burden of this activity. To understand this rule, affected entities would read the preamble and codified which together contain around 80,000 words. Following Health and Human Services guidelines, we calculate the cost of reading and understanding the proposed rule, if finalized, by assuming that industry reviewers read at the average adult reading speed of approximately 200 words to 250 words per minute (Ref. [2]). We estimate that the time to read the proposed rule, if finalized, would be 5.3 hours to 6.7 hours per person. We assume that 1 to 3 people would read the rule at each affected entity. To create a wider range of estimates, we assume a slower reading rate for those entities at which more people would need to read the rule.

To value the time for complying with reading and understanding the rule, we use composite wages calculated from the Bureau of Labor Statistics' (BLS) National Occupational Employment Statistics (OES) Industry-Specific Occupational Employment and Wage Estimates for the pharmaceutical and medicine manufacturing industry in May 2022 (Ref. [3]).[9] To value the time associated with reading and understanding the rule, we use a mix of 50 percent

[9] We use estimates from NAICS 325400 because detailed estimates for NAICS 325412 are not available.

managers (occupation code 11-0000) and 50 percent lawyers (occupation code 23-0000). This mix yields a composite wage of $88.95.[10] We double this wage to account for benefits and overhead, yielding a fully-loaded hourly labor cost of $177.89.

We estimate that the cost for 1 person to read the rule would range from $949 to $1,186. For each affected entity, these costs range from $949 to $3,558. We estimate that 78 sponsors of approved new animal drug applications would need to read and understand the rule. Therefore, the total costs for reading and understanding the rule would range from $74,002 to $277,508 in year 0. Table 9 presents a summary of these costs.

Table 9. One-time Costs for Reading and Understanding the Rule

	Low	Primary	High
Reading time per person (hours)	5.3	6.0	6.7
Labor cost ($ per hour)	$177.89	$177.89	$177.89
Affected entities	78	78	78
Number of people reading per entity	1	2	3
Total cost	$74,002	$166,505	$277,508

b. Establishing or revising industry labeling SOPs

Affected entities may respond to the proposed rule, if finalized, by establishing or revising SOPs related to labeling. We estimate that this activity would take 4 hours for small entities and 8 hours for large entities. The 2017 Statistics of U.S. Businesses data allow us to estimate the number of small firms in the pharmaceutical preparation manufacturing industry using a size threshold of 1,500 employees. Since approximately 93 percent of pharmaceutical preparation manufacturers have fewer than 1,500 employees, as we show in Table 2, we estimate that 72 of affected entities would be small.[11]

To value the time to establish or revise SOPs related to labeling, we use a mix of 20 percent upper managers (occupation code 11-1000), 70 percent middle managers (occupation code 11-2021), and 10 percent administrative workers (occupation code 43-0000). This mix yields a composite wage of $84.03.[12] We double this wage to account for benefits and overhead, yielding a fully-loaded hourly labor cost of $168.05.

We estimate that each small entity could incur costs of $672 and that each large entity could incur costs of $1,344 to establish or review SOPs for labeling. Therefore, the total one-time cost for affected entities would be $56,182 in year 0.[13] We summarize these costs in Table 10.

[10] The hourly wage for managers is $83.84, and the hourly wage for lawyers is $94.05. Therefore, this calculation is: (0.5 × $83.84) + (0.5 × $94.05) = $88.95.
[11] This equals 0.929 × 78.
[12] The hourly wage for upper managers (top executives) is $96.53, the hourly wage for middle managers (marketing managers) is $88.70, and the hourly wage for administrative workers (office and administrative support workers) is $26.31. Therefore, this calculation is: (0.2 × $96.53) + (0.7 × $88.70) + (0.1 × $26.31) = $84.03.
[13] This equals $127,951 + $19,706.

Table 10. One-time Costs for Establishing or Revising Labeling SOPs

	Small firms	Large firms
Time per entity (hours)	4	8
Labor cost ($ per hour)	$168.05	$168.05
Number of entities	72	6
Total cost	$48,684	$7,498

c. Training

We include a cost estimate for training those employees of new animal drug sponsors who are responsible for drug labeling. New animal drug sponsors would need to make them aware of newly established SOPs or revisions to SOPs due to labeling requirements of the proposed rule, if finalized. We estimate that the number of employees that each new animal drug sponsor would train would range from 1 to 3 based on the size of the sponsor. Also based on the size of the sponsor, we estimate that the number of training hours required per person would range from 1 to 4. We assume an equal employment type split between compliance officers and managers. We double the composite wage for these occupations to account for overhead costs.

The total one-time cost to industry to train employees would be $17,694 in year 0. We summarize costs for small and large firms in Table 11. We assume that the proposed rule, if finalized, would not result in recurring training costs, since we expect that new animal drug sponsors already account for routine training on labeling policies.

Table 11. Costs for Training

	Small firms	Large firms
Time per entity (hours)	1	12
Labor cost[a] ($ per hour)	$126.98	$126.98
Number of entities	72	6
Total cost	$9,196	$8,498

[a] The hourly wage for managers is $83.84, and the hourly wage for compliance officers (OES occupation code 13-1041) is $43.14. Therefore, the composite wage calculation is: (0.5 × $83.84) + (0.5 × $43.14) = $63.49. We double this value to calculate the fully loaded cost of labor.

2. Labeling change costs for approved applications

In this section, we estimate the costs of labeling changes due to the proposed rule, if finalized. To estimate these costs for proprietary labeling changes, we rely on the labor and materials costs to human drug sponsors for revising prescribing information and uploading revised labeling to our listing database from our regulatory impact analysis (RIA) for the "Content and Format for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling" final rule (hereafter referred to as "human prescription drug labeling RIA") (Ref. [4]). We recognize that these costs are imperfect proxies for the costs of proprietary labeling changes for new animal drugs and request comment on this approach.

a. Rx and OTC new animal drugs

We use the labor and materials costs from the human prescription drug labeling RIA to estimate the one-time costs of labeling changes for approved Rx new animal drug applications,

OTC new animal drug applications, and new animal drug applications that include both Rx and OTC animal drugs (Ref. [4]).[14]

To formulate our estimates, we adjust the labor and materials cost estimates from the human prescription drug labeling RIA from 2011 dollars to 2022 dollars. We update the materials costs in Table 10 of the human prescription drug labeling RIA to 2022 dollars using the Bureau of Economic Analysis GDP deflator.

In the human prescription drug labeling RIA, we estimate labor costs for regulatory affairs personnel and production personnel. To adjust these labor costs, we use May 2022 BLS OES wages to value the time spent revising labeling. To update the cost of labor for regulatory affairs personnel, we adopt the mean hourly wage for pharmacists (occupation code 29-1051) of $59.50. For production personnel, we use the mean hourly wage for first-line supervisors of production managers (occupation code 51-1011) of $37.72. We double these wages to account for benefits and overhead. We then calculate fully-loaded hourly labor costs of $119.00 for regulatory affairs personnel and $75.44 for production personnel. We multiply these hourly labor costs by the labor hours in Table 9 of the human prescription drug labeling RIA to estimate per labeling package revision costs to industry for Rx, OTC, and Rx/OTC new animal drugs (Ref. [4]).

Table 12 summarizes our estimates of labeling revision costs for small branded, medium branded, large branded, and generic new animal drug manufacturers.

Table 12. Per Labeling Package Revision Costs for Rx, OTC, and Rx/OTC New Animal Drugs in 2011 (2022 $)

	Small branded drug manufacturer	Medium branded drug manufacturer	Large branded drug manufacturer	Generic drug manufacturer
Labor cost	$2,444	$3,698	$5,555	$2,444
Materials cost	$791	$2,190	$3,137	$791
Total unit costs	$3,234	$5,888	$8,691	$3,234

We use CVM estimates of the number of Rx and OTC applications, as well as applications that have both Rx and OTC animal drugs, to estimate the number of labeling packages that manufacturers would modify. We estimate that, on average, Rx and OTC new animal drug applications include 2 labeling packages each, and applications with both Rx and OTC new animal drugs include 4 labeling packages each. Table 13 summarizes our estimates of the number of affected labeling packages in each compliance period.

[14] There is little to no difference between the costs to update Rx animal drug labeling and OTC animal drug labeling.

Table 13. Number of Affected Rx and OTC New Animal Drug Labeling Packages by Compliance Period

Product type	Compliance period	Count of NADAs	Count of ANADAs	Average number of labeling packages per application	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total number of labeling package changes
Rx	Year 1–2	91	9	2	182	18	200
	Year 2–3	70	72	2	140	144	284
	Year 3–4	38	45	2	76	90	166
	Year 4–5	38	47	2	76	94	170
	Year 5–6	26	22	2	52	44	96
OTC	Year 1–2	8	0	2	16	0	16
	Year 2–3	20	7	2	40	14	54
	Year 3–4	22	22	2	44	44	88
	Year 4–5	4	7	2	8	14	22
	Year 5–6	6	4	2	12	8	20
Rx/OTC	Year 1–2	0	0	4	0	0	0
	Year 2–3	1	0	4	4	0	4
	Year 3–4	2	0	4	8	0	8
	Year 4–5	1	1	4	4	4	8
	Year 5–6	0	0	4	0	0	0

We combine our estimates of labeling change costs and the number of labeling packages that manufacturers may need to modify to estimate the total costs of revising Rx and OTC new animal drug labeling due to the proposed rule, if finalized. We assume that sponsors of ANADAs would have the same costs for changing labeling as small manufacturers of NADAs for all cost estimates. In Table 14, we summarize the costs of changing Rx and OTC animal drug labeling to comply with this rule. Total costs to revise labeling for Rx and OTC new animal drugs across all compliance periods would range from $3.67 million to $7.29 million.

Table 14. Annual Rx and OTC New Animal Drug Labeling Change Costs

Product type	Compliance period	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total costs, low ($)	Total costs, primary ($)	Total costs, high ($)
Rx	Year 1–2	182	18	$646,881	$1,129,834	$1,640,064
	Year 2–3	140	144	$918,571	$1,290,073	$1,682,558
	Year 3–4	76	90	$536,911	$738,584	$951,647
	Year 4–5	76	94	$549,849	$751,521	$964,584
	Year 5–6	52	44	$310,503	$448,489	$594,269
OTC	Year 1–2	16	0	$51,750	$94,208	$139,063
	Year 2–3	40	14	$174,658	$280,801	$392,940
	Year 3–4	44	44	$284,628	$401,385	$524,738
	Year 4–5	8	14	$71,157	$92,386	$114,813
	Year 5–6	12	8	$64,688	$96,531	$130,173

Product type	Compliance period	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total costs, low ($)	Total costs, primary ($)	Total costs, high ($)
Rx/OTC	Year 1–2	0	0	$0	$0	$0
	Year 2–3	4	0	$12,938	$23,552	$34,766
	Year 3–4	8	0	$25,875	$47,104	$69,532
	Year 4–5	4	4	$25,875	$36,490	$47,703
	Year 5–6	0	0	$0	$0	$0
Total	All	662	474	$3,674,283	$5,430,959	$7,286,850

b. Proprietary labeling for Type A medicated articles and proprietary Type B and Type C medicated feeds

Because the proprietary labels for Type A medicated articles and proprietary Type B and Type C medicated feeds are similar to that of Rx and OTC new animal drugs, we use the same per labeling package cost estimates, as we show in Table 12. Table 15 summarizes the number of products that we would require to comply in each compliance period. Combination medicated feeds do not include proprietary labeling, and therefore we do not include this product type in Table 15.

Table 15. Number of Affected Labeling Packages with Proprietary Labeling for Type A Medicated Articles and Proprietary Type B and Type C Medicated Feeds by Compliance Period

Product type	Compliance period	Count of NADAs	Count of ANADAs	Average number of labeling packages per application	Number of labeling package changes
Type A medicated article	Year 1–2	5	0	1	5
	Year 2–3	6	4	1	6
	Year 3–4	14	3	1	14
	Year 4–5	12	1	1	12
	Year 5–6	19	5	1	19
Proprietary Type B medicated feeds	Year 1–2	0	0	1	0
	Year 2–3	0	0	1	0
	Year 3–4	1	0	1	1
	Year 4–5	1	0	1	1
	Year 5–6	0	0	1	0
Proprietary Type C medicated feeds	Year 1–2	0	0	3	0
	Year 2–3	3	0	3	9
	Year 3–4	7	0	3	21
	Year 4–5	18	0	3	54
	Year 5–6	1	0	3	3

We use these estimates to calculate the total proprietary labeling change costs in each compliance period for medicated articles and medicated feeds in Table 16. Total costs to revise proprietary labeling for medicated articles and medicated feeds across all compliance periods would range from $511,036 to $1.30 million.

Table 16. Annual Labeling Change Costs for Proprietary Labeling for Type A Medicated Articles and Proprietary Type B and Type C Medicated Feeds by Compliance Period

Product Type	Compliance period	Count of NADA labeling package changes	Count of ANADA labeling package changes	Total costs, low ($)	Total costs, primary ($)	Total costs, high ($)
Type A medicated article	Year 1–2	5	0	$16,172	$29,440	$43,457
	Year 2–3	6	4	$32,344	$48,266	$65,086
	Year 3–4	14	3	$54,985	$92,135	$131,384
	Year 4–5	12	1	$42,047	$73,890	$107,532
	Year 5–6	19	5	$77,626	$128,044	$181,310
Proprietary Type B medicated feeds	Year 1–2	0	0	$0	$0	$0
	Year 2–3	0	0	$0	$0	$0
	Year 3–4	1	0	$3,234	$5,888	$8,691
	Year 4–5	1	0	$3,234	$5,888	$8,691
	Year 5–6	0	0	$0	$0	$0
Proprietary Type C medicated feeds	Year 1–2	0	0	$0	$0	$0
	Year 2–3	9	0	$29,110	$52,992	$78,223
	Year 3–4	21	0	$67,922	$123,648	$182,521
	Year 4–5	54	0	$174,658	$317,952	$469,338
	Year 5–6	3	0	$9,703	$17,664	$26,074
Total	All	145	13	$511,036	$895,806	$1,302,308

c. Representative Type B and Type C medicated feed (Blue Bird) labeling

Animal drug manufacturers would update representative Type B and Type C medicated feed labeling (also known as Blue Bird labeling) in response to the proposed rule, if finalized. New animal drug sponsors create these labeling components for use by feed mills for labeling the medicated animal feeds that they produce. Representative Type B medicated feed labeling includes directions for mixing Type B medicated feeds into Type C medicated feeds, warnings, and other information. Representative Type C medicated feed labeling includes feeding directions, warnings, and other information that feed mills include on the final labels they create for Type C medicated feeds that they manufacture from Type A medicated articles or proprietary Type B medicated feeds and that will be complete and ready for animal consumption. Neither representative Type B nor Type C labeling for a resultant medicated feed is proprietary. It does not contain the name of a feed mill but serves as a template onto which a feed mill places its name and pertinent information for the safe and effective use of the product.

We estimate that new animal drug sponsors would spend 24 hours updating each Blue Bird labeling component associated with their application. We estimate that compliance officers would spend 20 hours and managers would spend 4 hours implementing these updates. Based on the May 2022 BLS OES wage data, the mean hourly wage for compliance officers (occupation code 13-1041) is $43.14, and the mean hourly wage for managers (occupation code 11-0000) is $83.84. We double these values to account for benefits and overhead, yielding fully-loaded

hourly labor costs of $86.28 for compliance officers and $167.68 for managers. Therefore, we estimate that the labor cost to update each Blue Bird labeling component would be $2,396.[15]

CVM estimates that, on average, there are 5 Blue Bird labeling components for each Type A medicated article application and each combination medicated feeds application. In addition, there is, on average, 1 Blue Bird labeling component per proprietary Type B medicated feed application. Table 8 contains our estimates of the number of affected Blue Bird labeling components by compliance period. We assume that animal drug manufacturers would update Blue Bird labeling on the same compliance schedule as for Type A medicated articles and proprietary Type B medicated feeds.

In Table 17, we estimate the costs in each year for required changes to the content and format of Blue Bird labeling.

Table 17. Blue Bird Labeling Change Costs by Compliance Period

	Year 1–2	Year 2–3	Year 3–4	Year 4–5	Year 5–6
Number of Blue Bird labeling components	25	70	276	336	465
Labor cost per labeling component ($)	$2,396	$2,396	$2,396	$2,396	$2,396
Total cost ($)	$59,908	$167,742	$661,384	$805,164	$1,114,289

d. Shipping labeling

We estimate costs for updating shipping and other labeling for each type of application separately from our other cost estimates. [16] Shipping and other labeling (hereafter referred to as "shipping labeling") provides minimal information about the drug and is simple in design. CVM has provided estimates of the average number of shipping labeling components for each type of application. We assume that, on average, each Rx and OTC new animal drug application contains 1 component of shipping labeling, each application that includes both Rx and OTC animal drugs contains 2 components, and every two Type A medicated article applications contain 1 component. We ask for comment on these assumptions and on relabeling costs for other labeling, including labeling on display cartons and multi-unit cartons. We assume that there would not be any shipping labeling costs for combination medicated feed applications or proprietary Type B or Type C medicated feed applications.

We estimate that new animal drug sponsors would spend 4 hours updating shipping labeling associated with each application. We estimate that compliance officers and managers would each spend 2 hours implementing these updates. Using the May 2022 BLS OES wage data, the mean hourly wage for compliance officers (occupation code 13-1041) is $43.14 and the mean hourly wage for managers (occupation code 11-0000) is $83.84. We double these wages to account for benefits and overhead, yielding fully-loaded hourly labor costs of $86.28 for compliance officers and $167.68 for managers. The estimated labor cost to update each component of shipping labeling is approximately $508. Table 18 summarizes our estimates of

[15] The calculation is: (20 × $86.28) + (4 × $167.68) = $2,396.

[16] Shipping and other labeling would, in general, exclude immediate container labels, secondary container labeling, and package inserts for Rx and OTC new animal drugs, and Type A medicated article labels, proprietary Type B and Type C medicated feed labels, and Blue Bird labeling.

the shipping labeling change costs in each compliance period by product type. Total costs to revise shipping labeling across all compliance periods would equal $306,022.

Table 18. Shipping Labeling Change Costs by Product Type

Product type	Compliance period	Count of applications	Shipping labeling changes per application	Cost per shipping labeling change	Total costs
Rx	Year 1–2	100	1	$507.92	$50,792
	Year 2–3	142	1	$507.92	$72,125
	Year 3–4	83	1	$507.92	$42,157
	Year 4–5	85	1	$507.92	$43,173
	Year 5–6	48	1	$507.92	$24,380
OTC	Year 1–2	8	1	$507.92	$4,063
	Year 2–3	27	1	$507.92	$13,714
	Year 3–4	44	1	$507.92	$22,348
	Year 4–5	11	1	$507.92	$5,587
	Year 5–6	10	1	$507.92	$5,079
Rx/OTC	Year 1–2	0	2	$507.92	$0
	Year 2–3	1	2	$507.92	$1,016
	Year 3–4	2	2	$507.92	$2,032
	Year 4–5	2	2	$507.92	$2,032
	Year 5–6	0	2	$507.92	$0
Type A medicated article	Year 1–2	5	0.5	$507.92	$1,270
	Year 2–3	10	0.5	$507.92	$2,540
	Year 3–4	17	0.5	$507.92	$4,317
	Year 4–5	13	0.5	$507.92	$3,301
	Year 5–6	24	0.5	$507.92	$6,095

3. Label change costs for feed mills to match new Blue Bird labeling

We do not include estimates of additional labor costs at feed mills for incorporating the updated representative labeling into sales and distribution software. This is because we expect feed mills to coordinate most of these updates with routine software updates. We request comment and data on the ability of feed mills to integrate these representative labeling updates in their sales and distribution software and any additional labor costs that feed mills could incur.

4. Costs to submit and review labeling supplements

The proposed rule, if finalized, would require new animal drug sponsors of affected applications to submit labeling changes as a supplement to their application. This requirement would impose additional labor costs that we do not account for in our labeling change estimates. We assume that sponsors would incur some labor costs to prepare and submit labeling supplements, and that FDA would incur costs to review labeling supplements.

The proposed rule, if finalized, would require new animal drug sponsors to submit updated labeling that conforms to the new requirements for an application in one supplement.[17] We assume that the information from new animal drug sponsors would require review by CVM before the sponsor could implement the conforming labeling. Therefore, we anticipate that labeling supplements would require up to 180 days of review by us.

We estimate that new animal drug sponsors would spend an average of 20 hours to prepare and submit the paperwork to support our approval of a labeling change. This estimate matches a previous FDA estimate of the burden for labeling and other changes to an approved application (Ref. [5]).[18] We assign these labor hours to medical and health services managers. The May 2022 BLS OES mean hourly wage for medical and health services managers (occupation code 11-9111) is $61.53. We double this wage to account for benefits and overhead, yielding a fully-loaded hourly labor cost of $123.06. We estimate that each labeling supplement would cost a new animal drug sponsor $2,461 to prepare.[19]

CVM estimates that reviewers have spent an average of 50 hours to review each labeling supplement based on data from fiscal year 2010 through fiscal year 2016. We assume that the conforming labeling for the proposed rule, if finalized, may take more time to review, because it would affect all labeling components and may affect more sections of the labeling. Therefore, we double this estimate and assume that CVM reviewers would need 100 hours to review each labeling supplement. We use 2022 data on FDA fully-loaded Full Time Equivalent (FTE) costs to estimate the fully-loaded hourly wage of staff from CVM ($139.55). Therefore, our cost to review 1 labeling supplement resulting from the proposed rule, if finalized, would be $13,955.[20]

We summarize our estimates of labor costs associated with submitting and reviewing labeling supplements in Table 19. Total costs to submit and review labeling supplements across all compliance periods would equal $13.59 million.

Table 19. Costs of Submitting and Reviewing Labeling Supplements by Compliance Period

Compliance period	Number of applications	Industry cost per application	FDA cost per application	Total cost ($)
Year 1–2	113	$2,461	$13,955	$1,855,025
Year 2–3	187	$2,461	$13,955	$3,069,820
Year 3–4	192	$2,461	$13,955	$3,151,901
Year 4–5	184	$2,461	$13,955	$3,020,572
Year 5–6	152	$2,461	$13,955	$2,495,255

[17] We charge user fees for an NADA or ANADA supplement only if the sponsor submits safety or effectiveness data. We do not anticipate the need for such data in supplements providing conforming labeling. Therefore, we do not expect to assess user fees for these labeling changes.
[18] See also OMB #0910-0032.
[19] This calculation is: 20 hours × $123.06 = $2,461.
[20] This calculation is: 100 hours × $139.55 = $13,955.

5. Costs for pending applications and applications submitted within 180 days of the effective date

a. Number of affected applications

The proposed rule, if finalized, would not require NADAs or CNADAs (including supplements) that are pending on the effective date of the final rule or that we receive during the first 180 days after the effective date of a rule to conform to the new labeling requirements in the initial application. However, the proposed rule, if finalized, would require such sponsors of nonconforming applications to submit conforming labeling to us in a supplement to the pending or approved application within 180 days of the date on which we approve the application.

To estimate the number of pending applications on the date we would publish the final rule and the number of applications that new animal drug sponsors would submit to us within 180 days of the final rule's effective date, we rely on data on NADA and ANADA submissions for the past 5 fiscal years (FYs). We refer to the FDA-TRACK Animal Drug User Fee Act (ADUFA) (Ref. [6]) and Animal Generic Drug User Fee Act (AGDUFA) (Ref. [7]) Drug Applications and Supplements data for fiscal years 2017 through 2021. The proposed rule, if finalized, would affect the following submission types:

- Original NADAs and reactivations
- Administrative NADAs and reactivations (including supplements)
- Major non-manufacturing supplemental NADAs and reactivations[21]
- Original ANADAs and reactivations
- Administrative ANADAs

For each submission type, we use (1) the length of the review period in days (which CVM provided to us) and (2) the average number of submissions we received per fiscal year for the last 5 fiscal years to calculate the average number of submissions that were pending per day and the average number of submissions that we received in a 180-day period. Based on these estimates, we assume that there would be approximately 8[22] pending NADAs and 15[23] pending ANADAs at the time of publication of the final rule. We also assume that in the first 180 days after we publish the final rule, we would receive 13 new NADA submissions and 11 new ANADA submissions. We present these data and estimates in Table 20.

Table 20. New Animal Drug Applications by Type over 5 Years

Submission type	Review period, days	FY 2017	FY 2018	FY 2019	FY 2020	FY 2021	5-year average	Pending per day[a]	Submitted within 180 days[b]
Original NADAs and reactivations	180	3	15	11	9	4	8.4	3.6	3.6

[21] Subject to 21 CFR part 514.8(c)(2)
[22] This equals 3.6 + 1.5 + 2.5.
[23] This equals 13.2 + 1.3.

Submission type	Review period, days	FY 2017	FY 2018	FY 2019	FY 2020	FY 2021	5-year average	Pending per day[a]	Submitted within 180 days[b]
Administrative NADAs and reactivations (including supplements)	60	16	18	8	11	9	12.4	1.5	4.5
Non-manufacturing supplemental NADAs and reactivations	180	6	10	2	4	9	6.2	2.5	2.5
Original ANADAs and reactivations	240	22	16	17	19	33	21.4	13.2	9.9
Administrative ANADAs	60	1	1	4	3	3	2.4	1.3	0.1

[a] To calculate these estimates, we divide the review period (in column 2) by 365 days and then multiply this value by the 5-year average (in column 8).
[b] To calculate these estimates, we divide the 5-year average (in column 8) by 2.03 (365 days divided by 180 days).

b. Number of affected labeling components

To distribute the estimated number of NADAs and ANADAs in Table 20 by product type, we apply the distribution of NADAs and ANADAs for approved and marketed new animal drugs by product type in Table 4 that we use to estimate labeling change costs in Section II.E.2. We display the distribution of approved NADAs and ANADAs by product type in Table 21.

Table 21. Percentage of Applications for Approved and Marketed New Animal Drugs by Product Type

Product type	Percentage of NADAs	Percentage of ANADAs
Rx	51.37%	61.71%
OTC	11.72%	12.66%
Rx/OTC	0.78%	0.32%
Type A medicated article	10.94%	4.11%
Combination medicated feeds	19.14%	21.20%
Proprietary Type B	0.39%	0.00%
Proprietary Type C	5.66%	0.00%

For pending applications and applications submitted within 180 days of the effective date of the final rule, the distribution of NADAs and ANADAs in Table 21 results in the estimated counts of NADAs and ANADAs by product type in Table 22. To estimate the number of proprietary labeling packages, Blue Bird labeling, and shipping labeling components that these applications would include, we refer to our assumptions from Section II.E.2 regarding the average number of labeling packages, Blue Bird labeling, and shipping labeling components per application.

We assume that, on average, each Rx application and OTC application would include 2 proprietary labeling packages; each Rx/OTC application would include 4 proprietary labeling packages; each Type A medicated article application and Proprietary Type B medicated feed application would include 1 proprietary labeling package; and each Proprietary Type C medicated feed application would include 3 proprietary labeling packages.

We further assume that, on average, each Type A medicated article application and combination medicated feeds application would contain 5 Blue Bird labeling components and each proprietary Type B medicated feed application would contain 1 Blue Bird labeling component. We assume that Rx and OTC applications would each contain 1 component of shipping labeling, Rx/OTC applications would each contain 2 components of shipping labeling, and every two Type A medicated article applications would contain 1 component of shipping labeling.

We display our estimates of the number of proprietary labeling packages, Blue Bird labeling, and shipping labeling components by product type in Table 22. In total, pending applications and applications that new animal drug sponsors would submit within 180 days of the effective date of the final rule would include approximately 65 proprietary labeling packages, 59 Blue Bird labeling components, and 32 shipping labeling components.[24]

Table 22. Estimated Proprietary Labeling Packages, Blue Bird Labeling, and Shipping Labeling Components for Pending Applications and Applications Submitted within 180 Days of Effective Date

Submission type	Product type	Estimated count of NADAs	Estimated count of ANADAs	Estimated NADA proprietary labeling packages	Estimated ANADA proprietary labeling packages	Estimated Blue Bird labeling components	Estimated shipping labeling components
Pending application	Rx	3.92	8.95	7.84	17.90	N/A	12.87
	OTC	0.89	1.84	1.79	3.67	N/A	2.73
	Rx/OTC	0.06	0.05	0.24	0.18	N/A	0.21
	Type A medicated article	0.83	0.60	0.83	0.60	7.15	0.72
	Combination medicated feeds	1.46	3.07	N/A	N/A	22.67	N/A
	Proprietary Type B	0.03	0.00	0.03	0.00	0.03	N/A
	Proprietary Type C	0.43	0.00	1.30	0.00	N/A	N/A
	Subtotal	7.63	14.50	12.02	22.35	29.86	16.52
Application submitted within 180 days of effective date	Rx	5.47	6.14	10.94	12.28	N/A	11.61
	OTC	1.25	1.26	2.50	2.52	N/A	2.51
	Rx/OTC	0.08	0.03	0.33	0.13	N/A	0.23
	Type A medicated article	1.17	0.41	1.17	0.41	7.87	0.79
	Combination medicated feeds	2.04	2.11	N/A	N/A	20.74	N/A
	Proprietary Type B	0.04	0.00	0.00	0.00	0.04	N/A
	Proprietary Type C	0.60	0.00	0.04	0.00	N/A	N/A
	Subtotal	10.65	9.95	14.98	15.34	28.66	15.14
Total	Rx	9.39	15.09	18.78	30.18	0.00	24.48
	OTC	2.14	3.10	4.28	6.19	N/A	5.24

[24] We calculate 65 proprietary labeling packages as the sum of 27.00 NADA labeling packages and 37.68 ANADA labeling packages.

Submission type	Product type	Estimated count of NADAs	Estimated count of ANADAs	Estimated NADA proprietary labeling packages	Estimated ANADA proprietary labeling packages	Estimated Blue Bird labeling components	Estimated shipping labeling components
	Rx/OTC	0.14	0.08	0.57	0.31	N/A	0.44
	Type A medicated article	2.00	1.01	2.00	1.01	15.03	1.50
	Combination medicated feeds	3.50	5.18	N/A	N/A	43.42	N/A
	Proprietary Type B	0.07	0.00	0.03	0.00	0.07	N/A
	Proprietary Type C	1.04	0.00	1.34	0.00	N/A	N/A
	Subtotal	18.28	24.45	27.00	37.68	58.51	31.66

c. Labeling change costs and costs to submit and review labeling supplements

We adopt the same cost assumptions for updating proprietary labeling packages, Blue Bird labeling, and shipping labeling components as in Section II.E.2. Following Section II.E.4, we additionally assume that new animal drug sponsors and FDA would incur costs to submit and review conforming labeling supplements, respectively. Specifically, we estimate that each labeling supplement would cost a new animal drug sponsor $2,461 to prepare and that our cost to review 1 labeling supplement would be $13,955.

It is likely that some new animal drug sponsors that submit initial applications or significant supplements to applications within 180 days after the effective date of the final rule would submit conforming labeling with their initial application. These sponsors would not incur any costs to update labeling to meet the labeling requirements in the proposed rule, if finalized. To construct a range of estimates, we assume that 0 percent to 100 percent of such sponsors would initially conform to the new labeling requirements, with a primary estimate of 50 percent. We request comment or data on this assumption.

For example, for our "primary" calculation of proprietary labeling change costs, we assume that sponsors would update approximately 27 NADA labeling packages at a cost of $5,888 per package and 38 ANADA labeling packages at a cost of $3,234 per package. If 50 percent of applications conform at the time of the initial submission, then total proprietary labeling change costs would equal $140,433.[25]

Given these assumptions, we present our estimates of costs for pending applications and applications submitted within 180 days of the effective date of the final rule in Table 23. We assume that industry and FDA would incur these one-time costs in year 0.

[25] This equals approximately: (27.00 × $5,887.99 × 0.50) + (37.68 × $3,234.40 × 0.50).

Table 23. Estimated Total Costs for Pending Applications and Applications Submitted within 180 Days of Effective Date

Cost type	Total costs, low ($)	Total costs, primary ($)	Total costs, high ($)
Proprietary labeling changes	$0	$140,433	$356,563
Blue Bird labeling changes	$0	$70,108	$140,215
Shipping labeling changes	$0	$8,040	$16,080
Submitting labeling supplements	$0	$52,584	$105,168
Reviewing labeling supplements	$0	$298,151	$596,303
Total costs, industry[a]	$0	$271,165	$618,027
Total costs, FDA[b]	$0	$298,151	$596,303

[a] This equals the sum of costs to industry from proprietary labeling changes, Blue Bird labeling changes, shipping labeling changes, and submitting labeling supplements.
[b] This equals the cost to FDA of reviewing labeling supplements.

6. Summary of costs over time

We assume that industry and FDA would incur costs at the beginning of each compliance period. That is, for the compliance period of year 5–6, we assume that industry and FDA would incur costs in year 5 for the purposes of calculating the present discounted value. At a 2 percent discount rate over 10 years, the annualized costs would range from $2.16 million to $2.77 million, and the present value of total costs would range from $19.78 million to $25.38 million (see Table 24).

Table 24. Discounted Costs of the Proposed Rule over 10 Years ($)

Year	Low (2%)	Primary (2%)	High (2%)
0	$147,878	$809,697	$1,565,714
1	$2,633,198	$3,161,314	$3,719,258
2	$4,320,047	$4,827,606	$5,363,831
3	$4,577,515	$4,987,603	$5,420,853
4	$4,385,170	$4,765,154	$5,166,598
5	$3,720,396	$3,927,092	$4,145,461
6	$0	$0	$0
7	$0	$0	$0
8	$0	$0	$0
9	$0	$0	$0
Present Value	$19,784,204	$22,478,465	$25,381,714
Annualized Value	$2,159,320	$2,453,382	$2,770,253

F. Benefits of the Proposed Rule

1. Cost savings from a reduction in the quantity and time burden of labeling amendments and informal communications related to labeling

We expect the standardized labeling content and format requirements in the proposed rule, if finalized, to result in cost savings to industry and FDA by reducing the quantity and time burden of labeling amendments to new animal drug applications and informal communications between industry and FDA relating to labeling.

a. Baseline costs for labeling amendments

Amendments correct mistakes or deficiencies in new animal drug submissions. Lack of clarity in the existing labeling requirements for new animal drugs may result in an excessive number of amendments to these submissions to correct labeling errors. We expect the proposed rule, if finalized, to result in cost savings to industry and FDA by reducing the number of labeling errors in—and, in turn, amendments to—new animal drug submissions due to unclear requirements. By centralizing labeling requirements in the CFR, the proposed rule, if finalized, is expected to reduce the amount of time it takes industry to prepare and submit, and FDA to review, any amendments to new animal drug submissions that include labeling revisions.

To estimate the magnitude of these cost savings, we first estimate the baseline annual costs to industry and FDA for labeling amendments. When submitting a labeling amendment, we assume that a sponsor incurs (1) costs to prepare and submit the amendment to FDA and (2) costs to revise labeling due to the amendment. We assume that FDA incurs costs to review the labeling amendments that industry submits to us. We estimate these costs separately.

In Section II.E.4, we assume that it takes industry an average of 20 hours to prepare and submit a new animal drug labeling supplement. We adopt the same assumption for labeling amendments. We multiply these labor hours by the May 2022 BLS OES fully-loaded hourly cost of labor for medical and health services managers ($123.06) to estimate the cost to industry to prepare and submit a single labeling amendment ($2,461).

To estimate the cost to industry to revise new animal drug labeling due to labeling amendments, we rely on the lower bound estimates of labor and materials costs for labeling revisions from the human prescription drug labeling RIA (Ref. [4]).[26] Based on Table 9 of the human prescription drug labeling RIA, we assume that it takes regulatory affairs personnel 18 hours and production personnel 4 hours to revise labeling for a single labeling amendment. We multiply these labor hours by the May 2022 BLS OES fully-loaded hourly labor costs for pharmacists ($119.00) and first-line supervisors of production managers ($75.44), respectively, to estimate the per amendment labor costs for regulatory affairs personnel ($2,142) and production personnel ($302). We add these values to calculate the per amendment labor cost to industry for labeling revisions ($2,444). We assume that the per amendment materials cost to industry for new animal drug labeling revisions equals $791 (the lower bound materials cost in Table 10 of the human prescription drug labeling RIA, converted to 2022 dollars).

[26] For these cost estimates, we do not make any assumptions regarding (1) the number of labeling amendments sponsors would submit per year for each product type or (2) which labeling components sponsors would revise as a result of submitted amendments. Instead, we calculate an average "per amendment" cost to industry to update labeling as a result of a labeling amendment.

We assume that it takes CVM reviewers 50 hours to review 1 new animal drug labeling amendment. This corresponds to the average review time for a single labeling supplement between fiscal years 2010 and 2016. We multiply these labor hours by the fully-loaded hourly wage of staff from CVM ($139.55) to estimate the cost to FDA to review a single new animal drug labeling amendment ($6,977).

We use CVM's Submission Tracking and Reporting System (STARS) to determine that FDA receives an average of 46 new animal drug labeling amendments per year.[27] We multiply the per amendment costs to industry and FDA by 46 to calculate the baseline annual costs to industry and FDA for new animal drug labeling amendments. We summarize these costs in Table 25.

Table 25. Baseline Costs to Industry and FDA for Labeling Amendments

Type of cost	Industry or FDA	Hours per amendment	Cost per amendment ($)	Annual cost ($)
Prepare and submit amendments	Industry	20	$2,461	$113,215
Revise labeling due to amendments (labor cost)	Industry	22[a]	$2,444	$112,413
Revise labeling due to amendments (materials cost)	Industry	N/A	$791	$36,370
Review amendments	FDA	50	$6,977	$320,964

[a] We allocate 18 hours to regulatory affairs personnel and 4 hours to production personnel.

b. Baseline costs for informal communications related to labeling

Informal communications are communications between FDA and industry prior to formally submitting a new animal drug application or amendment. By clarifying and centralizing labeling requirements, we assume that the proposed rule, if finalized, would reduce the number of informal communications related to labeling that industry initiates with us per year. We additionally assume that the time spent by industry to prepare and initiate, and FDA to respond to, each informal communication would decrease.

We estimate that CVM currently receives 46 informal communications related to new animal drug labeling per year.[28] We estimate that the labor burden for each informal communication ranges from 1 to 24 hours for both industry and FDA. We multiply the lower and upper burden per exchange by the fully-loaded hourly cost of labor for medical and health services managers to obtain the cost to industry per informal communication ($123 to $2,953). We multiply the lower and upper burden per exchange by the fully-loaded wage of staff from CVM to obtain the cost to us per informal communication ($140 to $3,349). We multiply these per communication costs by 46 to determine that the baseline annual cost for informal

[27] This corresponds to the average number of labeling amendments for (1) original and reactivated NADAs and substantial supplements; (2) original and reactivated ANADAs and substantial supplements; and (3) labeling minor technical section submissions to investigational new animal drug (INAD) and generic investigational new animal drug (JINAD) files that CVM received between 2017 and 2021. We exclude administration applications.

[28] We do not make any assumptions regarding the number of informal communications that sponsors would initiate per year for each product type.

communications related to labeling ranges from $5,661 to $135,858 for industry and from $6,419 to $154,063 for FDA.

c. Cost savings

We assume that the proposed rule, if finalized, would reduce the number of labeling amendments and informal communications that new animal drug sponsors submit to FDA each year by 15 percent. This represents a decrease in the number of annual new animal drug labeling amendments and informal communications related to new animal drug labeling to approximately 39. We also assume that the proposed rule, if finalized, would reduce the labor burden for new animal drug labeling amendments and informal communications by between 15 percent and 20 percent. We summarize costs to industry and FDA under these assumptions in Table 26.

Table 26. Costs to Industry and FDA for Labeling Amendments and Informal Communications Related to Labeling under the Proposed Rule

Action	Industry or FDA	Hours per submission, low	Hours per submission, high	Cost per submission, low ($)	Cost per submission, high ($)	Annual cost, low[a] ($)	Annual cost, high[a] ($)
Prepare and submit amendments	Industry	16	17	$1,969	$2,092	$76,986	$81,798
Revise labeling due to amendments (labor cost)	Industry	18[b]	19[c]	$1,955	$2,077	$76,441	$81,218
Revise labeling due to amendments (materials cost)	Industry	N/A	N/A	$791	$791	$30,914	$30,914
Review amendments	FDA	40	43	$5,582	$5,931	$218,255	$231,896
Initiate informal communications	Industry	0.85[d]	19[e]	$105	$2,363	$4,090	$92,384
Respond to informal communications	FDA	0.85	19	$119	$2,679	$4,638	$104,763

[a] We multiply the cost per submission by 39 to calculate total annual costs.
[b] This represents a 20 percent reduction in the labor burden for regulatory affairs personnel and production personnel in Table 25.
[c] This represents a 15 percent reduction in the labor burden for regulatory affairs personnel and production personnel in Table 25.
[d] This represents a 15 percent reduction in 1 hour.
[e] This represents a 20 percent reduction in 24 hours.

To calculate cost savings from a reduction in the quantity and time burden of labeling amendments, we subtract the costs to industry and FDA under the proposed rule from the baseline costs that we calculated in Section II.F.1.a. Annual cost savings to industry would range from $68,067[29] to $77,656.[30] Annual cost savings to FDA would range from $89,067 to

[29] This equals $31,417 + $31,195 + $5,455.
[30] This equals $36,229 + $35,972 + $5,455.

$102,708. We assume that these cost savings would begin to accrue in year 1. We summarize these cost savings in Table 27.

Table 27. Cost Savings to Industry and FDA from a Reduction in the Quantity and Time Burden of Labeling Amendments

Action	Industry or FDA	Baseline annual cost ($)	Annual cost under Proposed Rule, low ($)	Annual cost under Proposed Rule, high ($)	Annual cost savings, low[a] ($)	Annual cost savings, high[b] ($)
Prepare and submit amendments	Industry	$113,215	$76,986	$81,798	$31,417	$36,229
Revise labeling due to amendments (labor cost)	Industry	$112,413	$76,441	$81,218	$31,195	$35,972
Revise labeling due to amendments (materials cost)	Industry	$36,370	$30,914	$30,914	$5,455	$5,455
Review amendments	FDA	$320,964	$218,255	$231,896	$89,067	$102,708

[a] We subtract column 5 from column 3.
[b] We subtract column 4 from column 3.

To calculate cost savings from a reduction in the quantity and time burden of informal communications related to labeling, we subtract the costs to industry and FDA under the proposed rule from the baseline costs that we calculated in Section II.F.1.b. Annual cost savings to industry would range from $1,571 to $43,475. Annual cost savings to FDA would range from $1,781 to $49,300. We assume that these cost savings would begin to accrue in year 1. We summarize these cost savings in Table 28.

Table 28. Cost Savings to Industry and FDA from a Reduction in the Quantity and Time Burden of Informal Communications Related to Labeling

Action	Industry or FDA	Baseline annual cost, low ($)	Baseline annual cost, high ($)	Annual cost under Proposed Rule, low ($)	Annual cost under Proposed Rule, high ($)	Annual cost savings, low[a] ($)	Annual cost savings, high[b] ($)
Initiate informal communications	Industry	$5,661	$135,858	$4,090	$92,384	$1,571	$43,475
Respond to informal communications	FDA	$6,419	$154,063	$4,638	$104,763	$1,781	$49,300

[a] We subtract column 5 from column 3.
[b] We subtract column 6 from column 4.

2. Other potential benefits

Veterinarians, pet owners, and livestock owners need to locate and understand information contained on labeling in order to safely and effectively administer new animal drugs. The proposed rule, if finalized, would establish content and format requirements for new animal drug labeling within a given product category, which may lead to information search cost savings for users and benefit animal or human health. We discuss these potential benefits in more detail below. We request comment and data on the likelihood and magnitude of these benefits.

a. Information search cost savings

The proposed rule, if finalized, could reduce the amount of time it takes veterinarians and other users of new animal drugs, such as animal owners, to locate information on labeling, leading to information search cost savings.

Our current labeling requirements for prescription new animal drugs only specify that certain information must appear on labeling "on or within the package" from which the prescription new animal drug is dispensed.[31] However, these regulations don't provide direction on the format or order of information on labeling components for prescription new animal drugs, nor what minimal information new animal drug sponsors must provide on specific labeling components. There are currently no regulations that provide requirements for the general content and format of labeling for OTC new animal drugs or new animal drugs administered in animal feeds.

The lack of consistent requirements on the required format and order of information on all labeling for approved or conditionally approved new animal drugs can make it more difficult for users to look up information on animal drug labeling and add to the time it takes users to find the information they need.

Uncertainty in the amount of time that users of new animal drugs would save from standardized labeling content and format resulting from the proposed rule makes this benefit difficult to quantify. In Section II.G, we separately estimate the required time saved by veterinarians, pet owners, and livestock owners, respectively, for the annualized benefits of the proposed rule to equal the annualized costs.

b. Animal or human health benefits

New animal drug labeling that presents information in an inconsistent manner may contribute to medication errors by making it difficult for veterinarians and animal owners to readily locate and understand information that is important for the safe and effective use of a new animal drug. We expect the standardized content and format requirements in the proposed rule, if finalized, to help promote safe dispensing, administration, and use of approved or conditionally approved new animal drugs, and thus prevent medication errors. These new requirements could reduce the time and effort of users to readily identify and understand the risks and benefits of new animal drugs, thus enhancing users' ability to make informed decisions.

[31] These labeling requirements are in 21 CFR part 201.105.

In addition, the proposed rule, if finalized, would require that labeling for approved or conditionally approved new animal drugs contain contact information for consumers to report adverse events associated with the use of these new animal drugs. This may increase the likelihood that consumers will report adverse drug events to the sponsor or to CVM. Improving the ability to collect adverse event reports would allow new animal drug sponsors and CVM to more closely monitor and detect any new or emerging safety issues after new animal drugs are legally approved or conditionally approved and marketed. Any reduction in medication errors or improvement in adverse event reporting resulting from the finalization of the proposed rule would benefit animal or human health. We request comment and data on the extent to which the proposed rule, if finalized, would reduce medication errors, or improve adverse event reporting.

G. Breakeven Analysis

To estimate the required time saved by veterinarians, pet owners, and livestock owners for the annualized benefits of the proposed rule to equal the annualized costs, we make assumptions regarding the value of time to these populations and the sizes of these populations.

For veterinarians, we adopt the May 2022 BLS OES mean hourly wage for veterinarians (occupation code 29-1131) in the veterinary services industry (NAICS 541940) of $62.66. We double this wage to account for benefits and overhead, yielding an hourly labor cost for veterinarians of $125.32. Based on 2022 data from the American Veterinary Medical Association (AVMA), we assume that there are 124,069 employed veterinarians in the United States (Ref. [8]).

To quantify the hourly value of time for pet owners, we construct a range based on post-tax wages. The May 2022 BLS OES mean hourly wage for all occupations is $29.76.[32] We multiply $29.76 by the implied tax rate (25 percent) for household income, which we calculate from the Census Current Population Survey.[33] This results in a post-tax hourly value of time of $22.19. We estimate that the hourly value of time for pet owners ranges from $22.19 to $44.39 (double the post-tax wage), with a primary estimate of $33.29 (the average of the range). Based on a recent survey by the AVMA, we assume that approximately 71.48 million households own pets nationwide (Ref. [9]).[34]

For livestock owners, we adopt the May 2022 BLS OES mean hourly wage for first-line supervisors of farming, fishing, and forestry workers (occupation code 45-2093) in the support activities for animal production industry (NAICS 115200) of $25.48. We double this wage to account for benefits and overhead, yielding an hourly labor cost for livestock owners of $50.96. Based on statistics from the 2017 Census of Agriculture, there are 882,692 cattle operations,

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[32] See: https://www.bls.gov/oes/2022/may/oes_nat.htm.

[33] We use the procedure in the 2016 HHS Guidelines for Regulatory Impact Analysis (Ref. [2], footnote 73) to determine that the pre-tax mean household income in 2018 was $83,055 ($95,762 in 2022 dollars) and the post-tax mean household income in 2018 was $61,937 ($71,412 in 2022 dollars). Then, we calculate the implied tax rate as: ($95,762 − $71,412) ÷ $95,762.

[34] On December 31, 2016, 71,475,044 households owned at least one pet. The AVMA defines a "pet" as a dog, cat, bird, horse, or a specialty or exotic pet. Specialty and exotic pets include fish, ferrets, rabbits, hamsters, guinea pigs, gerbils, other rodents, turtles, snakes, lizards, other reptiles, other birds (pigeons and poultry), livestock and all other types of specialty and exotic animals that are kept as pets.

66,439 hog and pig operations, and 267,294 poultry farms in the United States (Ref. [10]). We assign one livestock owner to each of these farm units. Since some farms may include multiple species, we assume that the number of farm units—and livestock owners—nationally ranges from 882,692 to 1.22 million.[35]

We summarize our assumptions regarding the hourly value of time and population size for veterinarians, pet owners, and livestock owners in Table 29.

Table 29. Assumptions for Breakeven Analysis

Population	Hourly value of time	Population size, low	Population size, primary	Population size, high
Veterinarians	$125.32	N/A	121,461	N/A
Pet owners	$22.19	N/A	71,475,044	N/A
Livestock owners	$50.96	882,692	1,049,559	1,216,425

The total annualized net costs of the proposed rule, if finalized, over 10 years would range from $2.02 million to $2.53 million at a 2 percent discount rate, with a primary estimate of $2.26 million. To calculate the required time saved by veterinarians, pet owners, and livestock owners for annualized benefits of the proposed rule to equal annualized costs, we divide these net costs by the product of the hourly value of time and the population size for each population in Table 29. In Table 30, we present these estimates in minutes for veterinarians and livestock owners and in seconds for pet owners.

Table 30. Required Time Saved per Veterinarian, Pet Owner, or Livestock Owner per Year for Annualized Benefits to Equal Annualized Costs over 10 Years

Value	Low (2%)	Primary (2%)	High (2%)
Total annualized net costs of the Proposed Rule	$2,016,350	$2,260,232	$2,526,925
Required minutes saved per veterinarian	8	9	10
Required seconds saved per pet owner	2	3	6
Required minutes saved per livestock owner	1	1	1

Note: Estimates of required minutes saved per veterinarian, seconds saved per pet owner, and minutes saved per livestock owner in this table are exclusive of each other.

At a 2 percent discount rate, the primary estimate of the annualized costs of the proposed rule over 10 years would equal the annualized benefits if each veterinarian in the United States saves an average of 9 minutes per year.

At a 2 percent discount rate, the primary estimate of the annualized costs of the proposed rule over 10 years would equal the annualized benefits if each pet owner in the United States saves an average of 3 seconds per year.

[35] 1.22 million equals the sum of cattle operations, hog and pig operations, and poultry farms.

At a 2 percent discount rate, the primary estimate of the annualized costs of the proposed rule over 10 years would equal the annualized benefits if each livestock owner in the United States saves an average of 1 minute per year. Since we only account for owners of cattle, hogs and pigs, and poultry (and not owners of other types of livestock, such as sheep, goats, bison, cervids, and aquaculture), we may overestimate the amount of time that each livestock owner must save for the annualized benefits of the proposed rule to equal the annualized costs.

We request comment on whether and to what degree standardized content and format would save users time as they look for information on animal drug labeling.

H. International Effects

The proposed rule would affect all sponsors of new animal drugs approved or conditionally approved by the FDA no matter where the sponsors are located. In our analysis, we estimate the impacts of the proposed rule, if finalized, on all new animal drug sponsors. Foreign new animal drug sponsors may experience effects that are similar to those that we anticipate for domestic new animal drug sponsors. Therefore, we do not believe the proposed rule, if finalized, would alter the current mix of foreign and domestic new animal drug sponsors.

I. Analysis of Regulatory Alternatives to the Proposed Rule

1. Enact single compliance period

In this section, we alternatively quantify the impact of the proposed rule on costs if we were to enact a single compliance period of 6 years and a single compliance period of 2 years, respectively, for all affected applications and labeling components.

Instituting a universal 6-year compliance period would reduce the annualized costs of the proposed rule by $0.10 million at a 2 percent discount rate. Instituting a universal compliance period of 2 years would increase the annualized costs by $0.11 million at a 2 percent discount rate. In Table 31, we compare the discounted costs of the proposed rule to the discounted costs of each alternative.

Table 31. Costs of the Proposed Rule for Alternative Compliance Periods ($ millions)

Alternative	Present value (2%)	Annualized value (2%)	Change in annualized costs from Proposed Rule (2%)
Enact single compliance period of 6 years for all affected applications and labeling components	$24.48	$2.67	($0.10)
Proposed Rule	$25.38	$2.77	N/A

Alternative	Present value (2%)	Annualized value (2%)	Change in annualized costs from Proposed Rule (2%)
Enact single compliance period of 2 years for all affected applications and labeling components	$26.37	$2.88	$0.11

Note: Annualized costs are upper-bound costs discounted over 10 years. Estimates in parentheses are negative costs (e.g., are less costly than the proposed rule).

We are unable to quantify the impact of a universal compliance period on any information search cost savings to users of new animal drugs, or any human or animal health benefits resulting from the proposed rule, if finalized. However, instituting a universal 6-year compliance period would decrease the magnitude of any such impacts, and instituting a universal 2-year compliance period would increase the magnitude of any such impacts.

a. Enact single compliance period of 6 years

For this alternative, we assume that we would grant all affected applications that we have approved at the time of publication of the final rule 6 years from the effective date to comply with the new labeling requirements. We assume that industry and FDA would incur all labeling change costs for these applications in year 5.[36]

At a 2 percent discount rate over 10 years, the annualized cost of this alternative would range from $2.08 million to $2.67 million, and the present discounted cost would range from $19.07 million to $24.48 million.

b. Enact single compliance period of 2 years

Alternatively, we could require that all affected approved applications must comply with the new labeling requirements within 2 years of the effective date of the final rule. Under this alternative, industry and FDA would incur all labeling change costs for these applications in year 1.[37]

At a 2 percent discount rate over 10 years, the annualized cost of this alternative would range from $2.25 million to $2.88 million, and the present discounted cost would range from $20.63 million to $26.37 million.

c. Feasibility of alternatives

We do not believe that enacting a single compliance period of either 2 years or 6 years would be a feasible alternative to the proposed 5-year compliance schedule because it would

[36] Under a single compliance period of 6 years, we assume that industry and FDA would still bear one-time administrative costs, costs for pending applications, and costs for applications submitted within 180 days of the effective date of the final rule in year 0.

[37] Under a single compliance period of 2 years, we assume that industry and FDA would still bear one-time administrative costs, costs for pending applications, and costs for applications submitted within 180 days of finalization of the proposed rule in year 0.

create an undue burden on industry and FDA. Requiring sponsors of the newest approved NADAs to conform to the new requirements first, as we are proposing, would provide sponsors and FDA with adequate time and opportunity to reallocate resources, update SOPs, and fully adapt to the new requirements before implementing the likely more extensive labeling revisions to older approved NADAs.

2. Delay onset of compliance schedule

Rather than enacting a single compliance period for approved new animal drugs, we could delay the onset of the 5-year compliance schedule by moving the effective date forward in time. This would give all products more time to conform, while allowing compliance to still take place over 5 years.

As we show in Table 3, we currently assume that the most recently approved new animal drugs would conform in year 1 and the oldest products would conform in year 5. Shifting this compliance schedule forward in time (e.g., to years 2–6 or years 3–7) would decrease annualized compliance costs to industry and annualized costs to FDA to review labeling supplements. However, this would also delay the onset of any information search cost savings, and animal or human health benefits resulting from the proposed rule, if finalized.

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. This analysis, together with other relevant sections of this document and the preamble of the proposed rule, serves as the Initial Regulatory Flexibility Analysis, as required under the Regulatory Flexibility Act.

To assess the impact of the proposed rule on small entities, we compare the net costs of the proposed rule to industry to average annual revenues by firm size category. Because quantified effects of the proposed rule are estimated to be less than 2 percent of average annual revenues for the smallest firms, we propose to certify that the proposed rule, if finalized, would not have a significant economic impact on a substantial number of small entities. Therefore, we do not provide additional options to the proposed regulation. We request comment on our determination and possible alternatives to consider.

A. Description and Number of Affected Small Entities

The proposed rule, if finalized, would apply to any small sponsors of approved or conditionally approved new animal drugs. The costs to update labeling and submit labeling supplements that sponsors of approved and marketed new animal drugs would incur represent the largest share of total compliance costs to industry.[38] We therefore only present the costs to small sponsors of approved and marketed new animal drugs in this section.

[38] Our upper bound estimate of total compliance costs to industry annualized over 10 years is $1.50 million, which includes $1.41 million in costs to update labeling and submit labeling supplements for approved and marketed new animal drugs (estimated in Sections II.E.2 and II.E.4).

The U.S. Census Bureau designates animal drug manufacturers as "pharmaceutical preparation manufacturers" (NAICS 325412). The Small Business Administration size threshold for small pharmaceutical preparation manufacturers is 1,300 employees (Ref. [11]). Data from the U.S. Census Bureau's 2017 Statistics of U.S. Businesses allow us to estimate the number of small firms in the pharmaceutical preparation manufacturing industry using a size threshold of 1,500 employees.[39]

The 2017 SUSB data indicate that 935 pharmaceutical preparation manufacturing firms with employees have fewer than 1,500 employees (Ref. [1]). These data also show that there are 1,007 pharmaceutical preparation manufacturers in total. Using this information, we estimate that approximately 93 percent of pharmaceutical preparation manufacturers are small.[40]

B. Description of the Potential Impacts of the Rule on Small Entities

We estimate that there are 66 unique sponsors of approved and marketed new animal drugs based on internal data from CVM. We estimate that 39 of these sponsors operate domestically. Given our assumption from Section III.A that approximately 93 percent of these entities are small, we estimate that approximately 36 domestic sponsors of approved and marketed new animal drugs are small entities.

Our upper-bound estimate of annualized net compliance costs for sponsors of approved and marketed new animal drugs—accounting for both large and small firms, foreign and domestic—at a 2 percent discount rate over 10 years is $1.09 million.[41] For this estimate, we assume that sponsors of approved and marketed new animal drugs would experience 100 percent of the costs to update labeling and prepare labeling supplements for approved and marketed applications, and 85 percent of the other costs and cost savings to industry.[42] We further assume that the sponsors of approved and marketed new animal drugs operating domestically would incur 59 percent of these net compliance costs, or $643,956.[43]

In general, we expect that the proposed rule would require small entities to update fewer products and labeling than larger entities. However, we do not have enough information to directly estimate the number of products and labeling components associated with small new animal drug sponsors. Therefore, we assume that the percentage of total net compliance costs that small domestic sponsors of approved and marketed new animal drugs would bear would equal the percentage of new animal drug sponsors that are small.

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[39] This is the most recent year for which this detailed information is available.
[40] This equals 1,007 ÷ 935.
[41] These net costs include $1.41 million in costs to update labeling and prepare labeling supplements, $89,527 in additional costs, and $412,466 in cost savings.
[42] Eighty-five percent of affected firms have approved and marketed new animal drugs (66 firms ÷ 78 firms = 85 percent).
[43] Fifty-nine percent of firms with approved and marketed new animal drugs operate domestically (39 firms ÷ 66 firms = 59 percent).

We estimate that small domestic entities could incur up to $597,914 in annualized net compliance costs.[44] We distribute these costs among different sized entities based on the percentage of firms in each size category in the 2017 SUSB data. We then compare these compliance costs to the estimated annual revenue in each size category. In Table 32, we summarize the potential impacts of the proposed rule for small domestic sponsors of approved and marketed new animal drugs.

Table 32. Net Compliance Costs and Estimated Annual Revenues for Small Domestic Sponsors of Approved and Marketed New Animal Drugs

Employment size category	Number of firms	Percentage in size category	Annual receipts ($000)	Estimated compliance cost in size category	Compliance cost as a percentage of annual revenue
0 to 4	13	33%	$17,919	$211,668	1.181%
5 to 9	5	14%	$17,419	$86,969	0.499%
10 to 19	4	11%	$46,400	$71,622	0.154%
20 to 99	7	19%	$155,994	$122,780	0.079%
100 to 499	5	12%	$384,079	$77,377	0.020%
500 to 999	1	3%	$267,635	$20,463	0.008%
1,000 to 1,499	0	1%	$85,593	$7,034	0.008%
1,500+	3	7%	$6,094,790	$46,043	0.001%
Total small	36	93%	$975,039	$597,914	0.061%
Total	39	100%	$7,069,829	$643,956	0.009%

As we show in Table 32, entities in the smallest employment size categories may incur annualized costs of up to 1.18 percent of their annual revenues. Therefore, we propose to certify that the proposed rule would not have a significant economic impact on a substantial number of small entities. We request comment on this assumption and on our estimated costs.

IV. References

References with asterisks are not on public display at https://www.regulations.gov because they have copyright restriction. Some may be available at the website address, if listed. References with asterisks are available for viewing only at the Dockets Management Staff. 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.

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