



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 514

[Docket No. FDA-2012-N-0447]

RIN 0910-AG45

Antimicrobial Animal Drug Sales and Distribution Reporting

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA or we) is issuing a final rule to require that the sponsor of each approved or conditionally approved new animal drug product that contains an antimicrobial active ingredient submit an annual report to us on the amount of each such ingredient in the drug product that is sold or distributed for use in food-producing animals, including information on any distributor-labeled product. This final rule codifies the reporting requirements established in section 105 of the Animal Drug User Fee Amendments of 2008 (ADUFA). The final rule also includes an additional reporting provision intended to enhance our understanding of antimicrobial new animal drug sales intended for use in specific food-producing animal species and the relationship between such sales and antimicrobial resistance.

DATES: This rule is effective [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. For the applicable compliance dates, please see section V, “Effective and Compliance Dates” in SUPPLEMENTARY INFORMATION.

ADDRESSES: For access to the docket to read background documents or comments received, go to <http://www.regulations.gov> and insert the docket number found in brackets in the heading

of this final rule into the “Search” box and follow the prompts, and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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SUPPLEMENTARY INFORMATION:

Table of Contents

I. Executive Summary

A. Purpose of the Final Rule

B. Summary of the Major Provisions of the Final Rule

C. Legal Authority

D. Costs and Benefits

II. Background

A. Need for the Regulation/History of the Rulemaking

B. Summary of Comments to the Proposed Rule

C. General Overview of the Final Rule

III. Legal Authority

IV. Comments on the Proposed Rule and FDA Response

A. Introduction

B. Description of General Comments and FDA Response

C. Comments on our Legal Authority and FDA Response

D. Specific Comments and FDA Response

V. Effective and Compliance Dates

VI. Economic Analysis of Impacts

VII. Analysis of Environmental Impact

VIII. Paperwork Reduction Act of 1995

IX. Federalism

X. References

I. Executive Summary

A. Purpose of the Final Rule

The purpose of this rulemaking is to change the way we collect and report information related to the distribution and sale of approved or conditionally approved antimicrobial new animal drug products for use in food-producing animals.

Sponsors of approved or conditionally approved applications for new animal drugs containing an antimicrobial active ingredient are required by section 512 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360b), as amended by section 105 of ADUFA (ADUFA 105) (Title I of Pub. L. 110-316), to submit to us an annual report on the amount of each such ingredient in the drug that is sold or distributed for use in food-producing animals. We are also required by ADUFA 105 to publish annual summary reports of the data we receive from animal drug sponsors. In accordance with the law, sponsors of the affected antimicrobial new animal drug products began submitting their sales and distribution data to us on an annual basis, and we have published summaries of such data for each calendar year beginning with 2009. Since that time, we have published two documents inviting public input on

potential changes to our regulations relating to records and reports for approved new animal drugs, including an advance notice of proposed rulemaking (77 FR 44177, July 27, 2012) and a proposed rule (80 FR 28863, May 20, 2015). This final rule amends our existing records and reports regulation in part 514 (21 CFR part 514) to incorporate the sales and distribution data reporting requirements specific to antimicrobial new animal drugs that were added to the FD&C Act by ADUFA 105. ADUFA 105 was enacted to assist us in our continuing analysis of the interactions (including drug resistance), efficacy, and safety of antimicrobials approved for use in both humans and food-producing animals for the purpose of mitigating the public health risk associated with antimicrobial resistance. This rule includes an additional reporting provision intended to improve our understanding of antimicrobial animal drug sales intended for use in specific food-producing animal species. This additional provision assists us in assessing antimicrobial sales trends in the major food-producing animal species and examining how such trends may relate to antimicrobial resistance.

Finalizing this rule will assist us in assessing the rate at which sponsors are voluntarily revising their FDA-approved labeled use conditions to promote the judicious use of medically important antimicrobial drugs in food-producing animals. In December 2013, we published guidance for industry (GFI) #213 (<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf>), a guidance that calls on sponsors of approved medically important antimicrobial new animal drugs administered through medicated feed or water to voluntarily make changes to remove production uses (growth promotion and feed efficiency) from their product labels and bring the remaining therapeutic uses of these products (to treat, control, or prevent disease) under the oversight of a veterinarian by the end of December 2016. All affected

drug sponsors committed to implementing the changes described in guidance for industry (GFI) #213 by the December 2016 target date. Once the changes are fully implemented, it will be illegal to use these medically important antibiotics for production purposes, and animal producers will first need to obtain authorization from a licensed veterinarian to use them for therapeutic purposes (i.e., prevention, control, or treatment of a specifically identified disease).

Finalizing this rule also implements Sub-Objective 2.4.2 (“Enhance collection and reporting of data regarding antibiotic drugs sold and distributed for use in food-producing animals”) of the “National Action Plan for Combating Antibiotic-Resistant Bacteria” (National Action Plan) (https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf). The National Action Plan, released by the White House on March 27, 2015, was developed in response to Executive Order 13676: Combating Antibiotic-Resistant Bacteria, which was issued by President Barack Obama on September 18, 2014, in conjunction with the National Strategy for Combating Antibiotic-Resistant Bacteria. The National Action Plan is intended to guide the activities of the U.S. Government as well as the actions of public health, health care, and veterinary partners in a common effort to address the urgent and serious public health threat of drug-resistant bacterial infections. Objective 2.4 of the National Action Plan is to “enhance monitoring of antibiotic-resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain from food-animals on-farm, through processing, and retail meat.”

The provisions included in this final rule take into account stakeholder input received in response to multiple opportunities for public comment, including the advance notice of proposed rulemaking and the proposed rule.

B. Summary of the Major Provisions of the Final Rule

The rule amends the records and reports regulation in part 514 to include the following:

- Procedures relating to the submission to us of annual sales and distribution data reports by sponsors of approved or conditionally approved antimicrobial new animal drug products sold or distributed for use in food-producing animals. Sponsors are already submitting such reports as required by ADUFA 105.
- Procedures relating to the requirement for sponsors of approved or conditionally approved antimicrobial new animal drugs to begin submitting species-specific estimates of product sales as a percentage of their total sales. This new reporting requirement was included based on our authority under section 512(l)(1) of the FD&C Act.
- Procedures applicable to our preparation and publication of summary reports on an annual basis based on the sales and distribution data we receive from sponsors of approved or conditionally approved antimicrobial new animal drug products. The final rule includes specific parameters for the content of the annual summary reports as well as provisions intended to protect confidential business information and national security, consistent with ADUFA 105 and this Agency's regulations at § 20.61 (21 CFR 20.61).
- Provisions that will give sponsors of approved or conditionally approved antimicrobial new animal drug products that are sold or distributed for use in food-producing animals the opportunity to avoid duplicative reporting of product sales and distribution data to us under part 514.

C. Legal Authority

Our legal authority for issuing this final rule is provided by section 512(l) of the FD&C Act relating to records and reports concerning approved and conditionally approved new animal

drugs. In addition, section 701(a) of the FD&C Act (21 U.S.C. 371(a)) gives us general rulemaking authority to issue regulations for the efficient enforcement of the FD&C Act.

D. Costs and Benefits

We estimate one-time costs to industry from this final rule at about \$134,600. We estimate annual costs at about \$57,300. These costs equate to an estimated total annualized cost of about \$76,500 at a 7 percent discount rate over 10 years and about \$73,100 at a 3 percent discount rate over 10 years. The total annualized costs include the administrative cost to review the rule (\$8,800), plus the cost to those sponsors who wish to avoid duplicative reporting requirements under part 514 (\$4,900), plus the cost of providing the species-specific estimates of the percent of the drug product distributed domestically (\$62,700).

The final rule provides some flexibility in terms of the manner in which new animal drug sponsors report sales and distribution data under both § 514.80(b)(4) and § 514.87, by allowing the sponsor the option to satisfy its obligations under both provisions by making only one set of report submissions under certain circumstances. We estimate this will reduce labor costs for new animal drug sponsors by \$103,200 annually.

Another benefit of the final rule is the cost savings associated with sponsors reporting their monthly sales and distribution data to us in terms of product units rather than calculating the amount of antimicrobial active ingredients associated with these monthly product sales and distribution data, as is currently the case. We estimate the calculation reductions will amount to an annual benefit to animal drug sponsors of about \$19,100. We estimate total annual benefits to industry at about \$122,300.

II. Background

A. Need for the Regulation/History of the Rulemaking

Section 512(l)(1) of the FD&C Act, which was added by the Animal Drug Amendments of 1968 (Pub. L. 90-399), requires sponsors of approved or conditionally approved new animal drugs to establish and maintain records and make such reports of data relating to experience and other data or information received or obtained by the sponsor with respect to such drug as required by regulation or order. Part 514 of FDA's regulations implements section 512(l) of the FD&C Act and requires new animal drug sponsors to report various types of information to FDA relating to their approved drug products, including periodic drug experience reports under § 514.80(b)(4). Such reports must contain detailed information as specified in the regulations, including information concerning the quantities of the animal drug product distributed under the sponsor's approved application. The requirement for periodic reports under § 514.80(b)(4) applies to all sponsors of approved new animal drug products and is separate from the reporting requirements subsequently established under ADUFA 105 relating to antimicrobial new animal drugs.

This continuous monitoring of approved new animal drug applications (NADAs) by collecting post-approval information from sponsors is important because data previously submitted to FDA as part of the approval process may no longer be adequate, as animal drug effects can change over time and less apparent effects including, for example, on antimicrobial resistance, can sometimes take years to become evident. For this reason, post-approval reports are one of the primary means by which FDA can obtain information regarding safety or effectiveness problems with marketed new animal drugs.

In an effort to address mounting public health concerns about antimicrobial drug resistance, Congress, in 2008, enacted ADUFA 105 to enhance the reports collected by FDA concerning marketed new animal drug products that contain an antimicrobial active ingredient. ADUFA 105 amended section 512(l) of the FD&C Act by adding section 512(l)(3). Under new section 512(l)(3) of the FD&C Act, sponsors of antimicrobial new animal drugs approved or conditionally approved for use in food-producing animals must submit to us on an annual basis a report specifying the amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals. Specifically, sponsors are required to report the amount of each antimicrobial active ingredient as follows: (1) By container size, strength, and dosage form; (2) by quantities distributed domestically and quantities exported; and (3) for each dosage form, a listing of the target animals, indications, and production classes that are specified on the approved label of the product. The information must be reported for the preceding calendar year, include separate information for each month of the calendar year, and be submitted to us each year no later than March 31. The statute also requires FDA to publish summary reports of the antimicrobial drug sales and distribution data collected from the drug sponsors on an annual basis, and further requires that such data be reported by antimicrobial class (section 512(l)(3) of the FD&C Act). In accordance with the law, sponsors of the affected antimicrobial new animal drug products began submitting their sales and distribution data to us on an annual basis, and we have published summaries of such data for each calendar year beginning with 2009.

In the Federal Register of May 20, 2015 (80 FR 28863), we proposed to amend our existing animal drug records and reports regulation in part 514 to incorporate the antimicrobial drug sales and distribution data reporting requirements established by ADUFA 105. We

proposed (80 FR 28863 at 28864) to amend part 514 to include administrative practices and procedures for sponsors of antimicrobial new animal drugs sold or distributed for use in food-producing animals who must report annually under section 512(l)(3) of the FD&C Act. We also proposed (80 FR 28863 at 28864) to collect species-specific data to assist us in assessing antimicrobial sales trends in the major food-producing animal species and examining how such trends may relate to antimicrobial resistance. We set forth the rationale that having the improved data would support our ongoing efforts to encourage the judicious use of antimicrobials in food-producing animals to help ensure the continued availability of safe and effective antimicrobials for animals and humans (80 FR 28863 at 28864).

We believe that on-farm use data also are needed to obtain additional information necessary to help gauge the success of antibiotic stewardship efforts and guide their continued evolution and optimization, and assess associations between antibiotic use practices and resistance. Shortly after we issued the proposed rule, in the Federal Register of August 20, 2015 (80 FR 50638), we published a notice announcing plans to hold a public meeting on September 30, 2015, which we jointly sponsored with the U.S. Department of Agriculture (USDA) and the Centers for Disease Control and Prevention (CDC) to obtain public input on possible approaches for collecting additional on-farm antimicrobial drug use and resistance data. Such additional data are intended to supplement existing information, including data on the quantity of antimicrobials sold or distributed for use in food-producing animals and data on antimicrobial use and resistance, for example, data collected under the National Animal Health Monitoring System (NAHMS) and the National Antimicrobial Resistance Monitoring System (NARMS). In the notice of public meeting, we explained that data from multiple sources are needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal

agriculture (80 FR 50638 at 50639). Taking into account the comments received from this public meeting, we are continuing to work with the USDA and the CDC in developing this plan to help ensure the continued availability of safe and effective antimicrobials for use in humans and animals. The information that we will receive under this final rule is part of this coordinated, interagency effort to assess and minimize antimicrobial resistance to help ensure the continued availability of safe and effective antimicrobial drugs for use in treating infectious disease in animals and humans.

B. Summary of Comments to the Proposed Rule

We received approximately 440 individual comments on the proposed rule from veterinary, feed manufacturing, and livestock production associations, as well as consumer advocacy groups and individuals, and a member of Congress. Some comments support our rulemaking and our ongoing efforts to address the problem of antimicrobial resistance, while others express concern about the manner in which data are going to be collected, interpreted, and used. Some comments offer suggestions for specific changes for us to consider making to the subject regulations.

C. General Overview of the Final Rule

This final rule amends our animal drug records and reports regulation at part 514 to include administrative practices and procedures for sponsors of antimicrobial new animal drugs sold or distributed for use in food-producing animals who must report annually under section 512(l)(3) of the FD&C Act. In addition, the rule includes a provision based on our broader authority under section 512(l)(1) that requires sponsors to report antimicrobial new animal drug sales intended for use in specific food-producing animal species. In this rulemaking, we finalize the provisions in the proposed rule.

III. Legal Authority

Our legal authority for issuing this final rule is provided by section 512(l) of the FD&C Act relating to records and reports concerning approved new animal drugs and section 701(a) of the FD&C Act. Section 512(l) gives FDA broad authority to collect information from sponsors concerning their approved or conditionally approved new animal drug products. Specifically, under section 512(l)(1) of the FD&C Act, animal drug sponsors with approved or conditionally approved NADAs must “make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A) [relating to extralabel use], and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section [authorizing FDA to withdraw approval of a new animal drug or revoke a license to manufacture medicated feed].” The statute provides for withdrawal of approval if FDA finds that new information shows that the drug is no longer shown to be safe for use under the approved conditions of use or the drug is ineffective for uses prescribed or recommended in the drug’s labeling (21 U.S.C. 360b(e)(1)).

Pursuant to its authority under section 512(l)(1) of the FD&C Act, FDA issued recordkeeping and reporting regulations relating to experience with approved new animal drugs. These regulations, which are found at part 514, include the requirement at § 514.80(b)(4) for animal drug sponsors to submit periodic drug experience reports to FDA every 6 months for the first 2 years following approval of their application and subsequently on an annual basis. The

periodic reports that sponsors are required to submit under § 514.80(b)(4) must include detailed information as specified in the regulations, including information concerning the quantities of the animal drug product distributed under the sponsor's approved application. The requirement for sponsors to submit distribution data to us under § 514.80(b)(4) predates the enactment of ADUFA 105.

In addition to the broad authority already granted to FDA under section 512(l)(1) of the FD&C Act, in 2008, Congress established additional reporting requirements under ADUFA 105 for sponsors of antimicrobial new animal drug products. These new reporting requirements, which are set out in section 512(l)(3) of the FD&C Act, did not require the Agency to issue implementing regulations first in order for them to take effect. With respect to approved or conditionally approved new animal drugs containing an antimicrobial active ingredient, section 512(l)(3)(A) through (C) of the FD&C Act requires sponsors of such products to submit an annual report to FDA on the "amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals, including information on any distributor labeled product" by March 31 of each year with separate data included for each month of the preceding calendar year. In addition, section 512(l)(3)(E) of the FD&C Act requires FDA to prepare summaries of the information reported by drug sponsors concerning their antimicrobial new animal drugs and to make those summaries available to the public. In accordance with ADUFA 105, sponsors of the affected antimicrobial new animal drug products have submitted their sales and distribution data to us, and we have published summaries of such data, for each calendar year since 2009.

In enacting ADUFA 105, Congress clarified that "[t]he reports required [to be submitted by animal drug sponsors] under section 512(l)(3) of the Federal Food, Drug, and Cosmetic Act,

as added by subsection (a) [of ADUFA 105], shall be separate from periodic drug experience reports that are required under section 514.80(b)(4) of title 21, Code of Federal Regulations.” (see subsection (c) of ADUFA 105).

Section 701(a) of the FD&C Act gives us general rulemaking authority to issue regulations for the efficient enforcement of the FD&C Act.

IV. Comments on the Proposed Rule and FDA Response

A. Introduction

This section summarizes comments we received in response to the proposed rule and our response to those comments. We received approximately 440 individual comments on the proposed rule by the close of the comment period, each addressing one or more topics. Approximately 400 of those comments resulted from write-in campaigns. Several of the comments were signed by more than one person or group. We received comments from veterinary, feed manufacturing, and livestock production associations, as well as consumer advocacy groups and individuals, and a member of Congress. Some comments support our rulemaking and our ongoing efforts to address the problem of antimicrobial resistance, while others express concern about the manner in which data are going to be collected, interpreted, and used. Some comments offer suggestions for specific changes for us to consider making to the subject regulations. We considered the comments we received in response to the proposed rule in preparing this final rule. After considering these comments, we are not making any changes to the codified language that was included in the proposed rule.

In sections IV.B. through IV.D., we describe the comments received on the proposed rule and provide our responses. To make it easier to identify the comments and our responses, the word “Comment,” in parentheses, appears before the comment’s description, and the word

“Response,” in parentheses, appears before our response. We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number and, in some cases, we have separated different subjects discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment’s value or importance or the order in which comments were received.

B. Description of General Comments and FDA Response

Many comments make general remarks supporting or opposing the proposed rule without focusing on a particular proposed provision. In the following paragraphs of this section, we discuss and respond to such general comments.

(Comment 1) Many comments from a variety of stakeholders, including veterinary, feed manufacturing, and animal production associations, drug manufacturing firms, as well as consumer advocacy groups and individuals, generally support our efforts aimed at gathering reliable information on the use of antimicrobials in food-producing animals, improving the manner in which that information is reported, enhancing our understanding of antimicrobial animal drug sales intended for use in specific food-producing animal species, and working alongside our Federal partners to share data for the purpose of minimizing antimicrobial resistance.

(Response 1) We appreciate the general support that the comments express. As noted in section II.A., this rulemaking is part of a larger effort to address the problem of antimicrobial resistance. The rule is expected to provide us with information on the sales of antimicrobials intended for use in food-producing animals, including information regarding the sales of these

products among the various animal species for which they are intended. Having species-specific estimates of product sales and distribution in the four major food-producing categories of animal species (cattle, swine, chickens, turkeys) will be important in supporting efforts such as NARMS, the national surveillance program that tracks trends related to antimicrobial resistance in food-producing animals and humans, and complement data on antimicrobial use collected under NAHMS. The data will also complement the data collection plan with the USDA and the CDC to obtain additional on-farm use and resistance data. The collection of data from multiple sources, including enhanced sales data, is needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal agriculture. Such information will further enhance our ongoing activities related to slowing the development of antimicrobial resistance to help ensure that safe and effective antimicrobial new animal drugs will remain available for use in human and animal medicine. We intend to continue working in collaboration with the USDA, the CDC, the pharmaceutical industry, veterinary organizations, animal producers, and other stakeholders to address this important public health issue.

C. Comments on our Legal Authority and FDA Response

(Comment 2) Some comments suggest that we lack the legal authority to require drug sponsors to report species-specific distribution estimates.

Specifically, one comment suggests that we lack authority under section 512(l)(3) of the FD&C Act, as added by ADUFA 105, to require species-specific distribution estimates. The comment suggests that the lack of express authority in section 512(l)(3) of the FD&C Act to require species-specific distribution estimates thus limits our broader authority relating to the collection of records and reports concerning experiences and other information with respect to

approved new animal drugs under 512(l)(1) of the FD&C Act, and precludes us from requiring the submission of species-specific distribution estimates under that provision as well.

Three comments suggest that in addition to lacking authority to require species-specific distribution estimates under section 512(l)(3) of the FD&C Act, we also lack authority under section 512(l)(1) of the FD&C Act because we have not made a “finding” that species-specific distribution estimates are necessary in order to facilitate a determination of whether there may be grounds for invoking the withdrawal provisions of the FD&C Act.

(Response 2) FDA acknowledges that section 512(l)(3) of the FD&C Act, as added by ADUFA 105, does not explicitly address species-specific distribution estimates. In requiring such estimates, we rely not on section 512(l)(3) but rather on our broader authority under section 512(l)(1) of the FD&C to collect information concerning approved and conditionally approved new animal drugs under a regulation or order issued by FDA. (See Section III. Legal Authority.) Section 512(l)(1) of the FD&C Act reads in relevant part, “In the case of any new animal drug for which approval of an application filed pursuant to subsection (b) or section 571 is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience ... and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for” withdrawal of approval of the new animal drug at issue. FDA therefore has the authority to establish reporting requirements applicable to approved or conditionally approved new animal drugs by regulation or order if it finds those requirements are necessary to enable it

to determine, or facilitate a determination, as to whether the drugs are no longer shown to be safe, are ineffective, or are otherwise subject to withdrawal under section 512(e) of the FD&C Act.

Based on its authority under section 512(l)(1) of the FD&C Act, in March 2003, FDA issued regulations requiring recordkeeping and reports concerning experience with approved new animal drugs at § 514.80. Under § 514.80(b)(4), sponsors that have approved applications for new animal drugs, including sponsors of antimicrobial new animal drug products, must submit periodic drug experience reports to FDA every 6 months for the first 2 years following approval and annually thereafter. These periodic drug experience reports must contain, among other things, various types of information about the distribution of the sponsor's drug, including data concerning the quantity of the drug distributed domestically and the quantity exported. The requirement in § 514.80(b)(4) for sponsors to submit detailed distribution data concerning their approved new animal drugs predates the enactment of ADUFA 105. In enacting ADUFA 105, Congress left intact the periodic reporting requirements under § 514.80(b)(4)--including the requirement for distribution data--stating at ADUFA section 105(c) that the reporting requirements established under section 512(l)(3) of the FD&C Act for antimicrobial new animal drugs did not relieve the sponsors of their separate obligation to provide periodic drug experience reports to FDA under § 514.80(b)(4). In so doing, Congress clearly signaled that the reporting requirements relating to antimicrobial drugs in 512(l)(3) were intended to supplement rather than supplant FDA's existing authority under section 512(l)(1) to impose distribution data reporting requirements on the same parties covered by section 512(l)(3) of the FD&C Act.

Further, the scant legislative history relating to ADUFA 105 that exists supports the conclusion that in establishing section 512(l)(3) Congress meant to enhance, not limit, our

general authority under section 512(l)(1) of the FD&C Act to require information about marketed new animal drug products in order to ensure their continued safety and effectiveness. For example, in his remarks to other members of Congress, Chairman of the House Energy and Commerce Subcommittee on Health, Representative Frank Pallone, Jr., stated that the ADUFA legislation he had introduced earlier that year would “improve the uniform collection and reporting of data to FDA on the sales about animal drugs that contain an antibiotic ingredient” and that it “includes language that would enhance FDA’s current data collection by creating a new antimicrobial animal drug use data report for all food-producing animals. The report puts critical information in one place for FDA; otherwise, the agency would have to search through warehouses of multiple paper reports.” 154 Congressional Record 17,287 (2008)(statement of Rep. Pallone). In remarks Representative Waxman made concerning the legislation, he stated, “The ADUFA bill we are considering includes a provision to increase the availability and accessibility of data on the amount of animal antibiotics being distributed” and that the “reauthorization [of ADUFA] has also given us an opportunity to look at providing FDA with new tools to address a related public health crisis, the problem of antibiotic resistance.” 154 Congressional Record 17,288 (2008) (statement of Rep. Waxman). These statements made by members of Congress strongly suggest that FDA was viewed as already having the requisite legal authority under section 512(l) and that the reason Congress established the requirement in section 512(l)(3) of the FD&C Act for an additional report relating to antimicrobial new animal drugs sold for use in food-producing animals was merely to improve the efficiency of the reporting process for such drugs so that we could more effectively address the problem of resistance associated with the use of antimicrobial drugs in food animal production. In addition to improving efficiency by establishing a more uniform process for the collection of important

information about approved antimicrobial new animal drugs sold or distributed for use in food-producing animals, ADUFA 105 also streamlined the process for putting these reporting requirements in place by eliminating the need for the Agency to first engage in time-consuming rulemaking activities that otherwise would have been required under section 512(l)(1) of the FD&C Act prior to collecting such data.

In light of what we consider to be clear evidence that Congress intended section 512(l)(3) of the FD&C Act to bolster rather than limit our existing authority to require information to be reported concerning approved new animal drugs, we conclude that the comment's assertion, that by establishing section 512(l)(3) Congress has somehow curtailed our ability to exercise authority we would otherwise have under section 512(l)(1), is without merit.

We now respond to the comments asserting that we may not rely on section 512(l)(1) of the FD&C Act absent a finding that species-specific distribution estimates are necessary in order to facilitate a determination of whether there may be grounds for invoking the withdrawal provisions of the FD&C Act. Although we stated in the proposed rule that collection of species-specific sales and distribution estimates would help to ensure "the continued availability of safe and effective antimicrobials for animals and humans," we agree that language more clearly stating our finding is appropriate. Accordingly, we find that the collection of species-specific sales and distribution estimates, in addition to other information about antimicrobial use in food-producing animals and drug resistance, is necessary to enable us to determine, or to facilitate a determination, as to whether there may be grounds for additional measures short of and, where appropriate, including withdrawal of approval or specific portions of the approval in certain instances in the future to minimize antimicrobial resistance and ensure the continued availability of safe and effective antimicrobials for use in treating animals and humans. In particular, such

information is needed, among other reasons, to support ongoing efforts to promote the judicious use of antimicrobials in food-producing animals and evaluate the success of those efforts; to aid in our assessment of antimicrobial sales trends in the major food-producing animal species and our examination of how these species-specific sales trends may relate to antimicrobial resistance; and to help inform microbial food safety risk assessments. In addition, because many antimicrobial drugs are approved for use in multiple species, in those instances where we believe appropriate grounds may exist to withdraw approval, having species-specific information also will be necessary to help us determine which specific portions of the approval may need to be withdrawn.

D. Specific Comments and FDA Response

Many comments make specific remarks supporting or opposing a particular proposed provision. In this section, we discuss and respond to such comments. The order of the discussion reflects the order in the regulatory text.

(Comment 3) Several comments support our effort to eliminate duplicative reporting of sales and distribution data by sponsors of antimicrobial new animal drugs.

(Response 3) We agree with the comments and therefore, in this final rule, we are keeping language as proposed at § 514.80(b)(4)(i)(B). As described in the proposed rule (80 FR 28863 at 28871), we are providing an opportunity for sponsors of antimicrobial new animal drugs to modify the reporting period for these drug products in order to eliminate duplicative reporting of quantity marketed under current § 514.80(b)(4) and new § 514.87.

(Comment 4) Several comments support reporting of sales and distribution data but suggest modification of the proposed requirement in § 514.87(a) and (b)(1) to report the antimicrobial active ingredient. One comment suggests that we reduce the scope of what we

require to be reported so that we only collect data for what it characterizes as “medically important antimicrobials.” Another comment suggests that we expand the scope of what we require to be reported to include data on what the comment characterizes as live cultures and complex products “intentionally developed and marketed for antimicrobial production.”

(Response 4) We have carefully considered the comments’ suggested changes to the scope of reporting of the antimicrobial active ingredient. The requirement to report the antimicrobial active ingredient under § 514.87(a) reflects the requirement, under section 512(l)(3) of the FD&C Act, for each sponsor of a new animal drug product that is approved or conditionally approved and contains an antimicrobial active ingredient, to report to us on an annual basis the amount of each antimicrobial active ingredient in the drug product that is sold or distributed for use in food-producing animals. This includes products that are the subject of an approved NADA or abbreviated NADA, as well as products that are conditionally approved under section 571 of the FD&C Act (21 U.S.C. 360ccc). The requirement in § 514.87(a) also incorporates the requirement from section 512(l)(3) of the FD&C Act for animal drug sponsors to capture in their sales and distribution data reports information regarding any distributor labeled products (see section 512(l)(3)(A) of the FD&C Act). We decline to implement the suggestion to limit the reporting to “medically important antimicrobials” due to the statutory reporting requirements under section 512(l)(3) of the FD&C Act, which apply to a new animal drug product that is approved or conditionally approved and contains an antimicrobial active ingredient without limitation.

With regard to the comment about live cultures and complex products, we understand the comment to be referring to products that contain one or more microorganisms. We carefully considered the issues the comment raises and are finalizing the proposed rule without change.

Currently, there are no approved new animal drug products that contain microorganisms and such products do not appear in Appendix A, GFI #152 as being important in human clinical medicine

(<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf>). A live culture or complex product could potentially be the subject of a NADA if because of its intended use the particular product at issue meets the statutory definition of a drug in section 201(g) of the FD&C Act (21 U.S.C. 321(g)) (an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease or an article (other than food) intended to affect the structure or any function of the body) and the statutory definition of a new animal drug in section 201(v) of the FD&C Act. Furthermore, should a live culture or complex product be approved as a new animal drug, and should any of the active ingredients of that product be approved specifically for an antimicrobial use or be known to have antimicrobial properties, then sponsors of such an approved product would be required to submit data to us on the amount of each such ingredient in this drug product sold or distributed for use in food-producing animals.

(Comment 5) Comments on the proposed rule generally support our effort to learn more about antimicrobial resistance, but several comments disagree with our proposal to collect species-specific estimates as proposed in § 514.87(c). Several comments question the utility of the information that would result from species-specific data. Several comments suggest that it was unclear how species-specific estimates will scientifically support NARMS, or complement NAHMS. Other comments state that species-specific sales estimates are inappropriate to report because the resulting data would not constitute sound scientific data. These comments assert that such data would be inaccurate due to complications and inconsistencies of data collection, would

not reflect actual usage, would be subject to misinterpretation due to lack of complete information, and would not constitute sufficient data to evaluate the impact of policies and trends in antimicrobial resistance. Other comments support our collection of species-specific sales and distribution data as proposed in § 514.87(c). These comments assert that the resulting data would be beneficial to understanding how antimicrobials are used in food-producing animals, the relationship between sales/use and antimicrobial resistance, and the impact of our policies and practices to mitigate antimicrobial resistance.

(Response 5) We have carefully considered the comments in favor of and opposing the reporting of species-specific sales and distribution data as specified in proposed § 514.87(c). We recognize the comments' concerns with regard to utility of the information but we respectfully disagree with the request to remove species-specific reporting from the rule. As we discussed in our response to Comment 1, having species-specific estimates of product sales and distribution for use in the four major food-producing categories of animal species (cattle, swine, chickens, turkeys) will be essential in supporting efforts to assess antimicrobial drug use and resistance in animal agriculture. This additional sales and distribution data will help inform microbial food safety risk assessments by providing a better indication of the extent to which a drug or drug class is used in a specific food animal species by a specific route of administration. Aggregate sales data do not provide this information and are more subject to misinterpretation.

As noted in our response to comment 1, we also intend to consider estimates of species-specific sales and distribution data in conjunction with on-farm species-specific data on antimicrobial use, such as that collected under NAHMS. We expect such data to help us better understand the extent of antimicrobial use in the various major food animal species and provide additional context as we examine resistance data, such as those collected under NARMS. Data

from multiple sources are needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal agriculture. Such information is critical to our ongoing activities related to slowing the development of antimicrobial resistance and ensuring the continued availability of safe and effective antimicrobials for use in treating animals and humans. For the reasons discussed here and in response to comments 1 and 2, we are retaining the requirement for sponsors to provide species-specific sales and distribution estimates as set forth in § 514.87(c).

(Comment 6) Several comments we received suggest that, instead of collecting species-specific sales estimates as proposed in § 514.87(c), antimicrobial use in food-producing animals should be monitored at the farm level. Some comments raise concerns about using sales data alone in analyses of antimicrobial drug use and resistance. There were multiple comments requesting that we collaborate with the USDA and the CDC to enhance existing collection efforts of on-farm antimicrobial use data that are accurate, detailed, and quantitative to supplement species-specific estimates of product sales. The commenters further request that we use the data to evaluate the impact of policies, understand the relationship between usage and resistance trends, and construct targeted interventions.

(Response 6) We disagree with the request to remove species-specific reporting from the rule for the reasons discussed in our responses to comments 1, 2, and 5. We recognize that gathering information on the way medically important antimicrobials are used in food-producing animals is essential to: (1) Assess the rate at which sponsors are voluntarily revising their FDA-approved labeled use conditions to promote the judicious use of medically important antimicrobial drugs in food-producing animals, (2) help gauge the success of antibiotic

stewardship efforts and guide their continued evolution and optimization, and (3) assess associations between antibiotic use practices and resistance.

We agree with the suggestion to collaborate with the USDA and the CDC to enhance existing collection efforts of on-farm antimicrobial use data. We are collaborating with the USDA and the CDC to develop a plan for collecting additional on-farm data on antimicrobial use and resistance. Such data are intended to supplement existing information, including data on the quantity of antimicrobials sold or distributed for use in food-producing animals (reported under § 514.87 as established under this final rule) and data on antimicrobial use and resistance, for example, data collected under the NAHMS and NARMS programs. Data from multiple sources are needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal agriculture and ensure the continued availability of safe and effective antimicrobials for use in treating animals and humans. Each source provides unique species-specific data; collecting species-specific sales and distribution data will support evaluation of other species-specific data, such as data collected under the NAHMS and NARMS programs.

As discussed in section I.A. Purpose of the Final Rule, in December 2013, we published GFI #213, a guidance that calls on sponsors of approved medically important antimicrobial new animal drugs administered through medicated feed or water to voluntarily make changes to remove production uses (growth promotion and feed efficiency) from their product labels and bring the remaining therapeutic uses of these products (to treat, control, or prevent disease) under the oversight of a veterinarian by the end of December 2016. The sales data collected under this final rule will assist us in assessing the rate at which sponsors are voluntarily revising their FDA-approved labeled use conditions to align with GFI #213.

As also discussed in section I.A., the National Action Plan, issued by the White House in March 2015, is intended to guide the activities of the U.S. Government as well as the actions of public health, health care, and veterinary partners in a common effort to address the urgent and serious public health threat of drug-resistant bacterial infections. Objective 2.4 of the National Action Plan is to enhance monitoring of antibiotic resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain for food animals and retail meat. Sub-Objective 2.4.3 of the National Action Plan calls for the USDA and FDA to seek public input on a plan for collecting drug use and resistance data on farms. We are continuing to work with both the USDA and the CDC to develop this plan. A joint public meeting was held on September 30, 2015, to provide an opportunity for public comment on possible approaches for collecting additional antimicrobial drug use data.

(Comment 7) Some comments suggest that, instead of or in addition to collecting the species-specific estimates that would be required as proposed in § 514.87(c), we should collect and report the information already provided in veterinary feed directive (VFD) orders and information related to these orders.

(Response 7) The VFD regulation outlines the process for authorizing use of VFD drugs (animal drugs intended for use in or on animal feed that require the supervision of a licensed veterinarian) and provides veterinarians in all States with a framework for authorizing the use of these VFD drugs, including medically important antimicrobials, when needed for specific animal health purposes. The VFD regulation provides that all distributors, regardless of whether or not they manufacture animal feeds bearing or containing VFD drugs, must keep records of receipt and distribution for 2 years from the date of issuance in accordance with 21 CFR 558.6(c)(3).

We appreciate the commenters' suggestions that we gather the information provided in VFD orders and information related to these orders. While there are some limitations to the gathering of such information, we agree that this information has value. For that reason, we continue to consider options to capture such information.

We believe that VFD records are an important source of information for assessing veterinary oversight of VFD drugs and compliance with the VFD regulation. These records are required to be made available to FDA during inspections. Therefore, as part of these inspectional activities, we intend to use these records to review compliance with the VFD regulations, to ensure that the VFD drug and VFD feed are used according to the conditions and indications of use as specified in the approval, conditional approval, or index listing, and within the supervision and oversight of a licensed veterinarian.

(Comment 8) One comment generally supports the collection of sales data, but suggests that we provide a specific methodology for making species-specific sales estimates to reduce the likelihood of inaccurate reporting of these estimates.

(Response 8) We appreciate the commenter's interest in obtaining the most accurate data and their suggestion that we identify a specific methodology for developing species-specific sales estimates. We appreciate and agree with the need to gather the best data. We also recognize that the sponsors who are required to report have different ways of managing their businesses, including different ways of capturing sales and distribution data. In other words, different sponsors gather sales data on similar drug products in different ways and, sometimes, the same sponsor may gather sales data on different drug products within their own drug product portfolio in different ways. Because of these differences, it seems likely that sponsors' methods of gathering these sales data will vary considerably.

We believe that animal drug sponsors currently have access to information obtained in the ordinary course of their business (for example, through proprietary marketing analyses) that can be used to formulate the methodology to estimate the percentage of annual product sales that are sold or distributed domestically for use in any of the four major food-producing species that appear on the approved product label. In addition, sponsors have different business models that determine the manner in which they gather sales data; thus, specific methodologies to accurately estimate species-specific sales will likely differ among sponsors. As we finalize this rule and establish the requirement that sponsors estimate species-specific sales for the major food-producing species, we recognize that specifying a uniform methodology for estimating species-specific sales might cause a firm to provide estimates in a manner not best suited to their individual business processes, leading the firm to expend more time to provide species-specific sales estimates that may be less accurate than those derived from utilizing their own methodology. The provision at § 514.87(c) requires that firms provide species-specific sales estimates. We expect these estimates to be based on the methodology that provides the sponsor's most accurate estimate of these sales.

Also, as we noted in the proposed rule, this provision is not intended to require animal drug sponsors to conduct studies of on-farm drug use practices (80 FR 28863 at 28866). For these reasons, we decline at this time to provide a standard methodology for developing species-specific sales estimates.

(Comment 9) One comment suggests that we should not collect the species-specific sales and distribution estimates that we proposed to require under § 514.87(c) until legal challenges over disclosure of confidential commercial information are resolved.

(Response 9) We have carefully considered the issues regarding the protection of confidential commercial information. As we stated in the proposed rule, “[s]ince it is likely that many sponsors would consider their species-specific sales and distribution estimates as proprietary information, and that such estimates may often be derived from proprietary marketing analyses, FDA would, as described in proposed paragraph (e) [of § 514.87], consider the species-specific information reported by individual sponsors under paragraph (c) [of § 514.87] to be confidential business information consistent with section 512 (l)(3) of the FD&C Act and this Agency’s regulations at 21 CFR 20.61.” (80 FR 28863 at 28867). In recognition of this concern, we further stated in the proposed rule that, consistent with the statute, FDA would not “independently report those antimicrobial classes with fewer than three distinct sponsors, and would further require that, in reporting the antimicrobial drug sales and distribution data it receives from drug sponsors, FDA must do so in a manner consistent with protecting both national security and confidential business information (see section 512(l)(3)(E)(i) and (ii) of the FD&C Act).” (80 FR 28863 at 28867.) After considering the comments received in response to the proposed rule, we conclude there are sufficient safeguards in place to ensure the protection of confidential commercial information, including the species-specific information required to be submitted by individual firms in accordance with § 514.87(c). Therefore, we are not removing the requirement for species-specific sales and distribution estimates under § 514.87(c) for confidentiality reasons as the comment requests and are finalizing the provision at § 514.87(e) relating to the confidentiality of sales and distribution data as proposed.

(Comment 10) One comment suggests that we modify proposed § 514.87(c) to include fish on the list of animal species categories for which sponsors are required to report species-specific estimates.

(Response 10) We carefully considered the suggestion to include fish on the list of animal species categories for which species-specific estimates must be submitted and decided to retain the categories that were identified in proposed § 514.87(c) without modification. We consider the most significant risk to the public health associated with antimicrobial resistance related to the use of antimicrobial drugs in animal agriculture to be human exposure to food containing antimicrobial-resistant bacteria resulting from the exposure of food-producing animals to antimicrobials. However, when considering the foodborne pathway, the potential for human exposure to antimicrobial-resistant pathogens currently is significantly less for food derived from minor species than it is for food derived from the food-producing major species. The exposure potential is less in part because the amount of food derived from cattle, swine, and poultry is much greater than the amount of food derived from sheep, goats, and aquaculture, the minor species from which the most food is derived (Refs. 1 and 2). In the United States, human foodborne illnesses are attributed mostly to plant and land animal commodities (Ref. 3). Furthermore, the majority of illnesses attributed to fish exposure are intoxications rather than bacterial illnesses (Ref. 4). Additionally, most fish and seafood consumed in the United States are imported products (Ref. 5).

In addition, as discussed in the proposed rule, we believe having species-specific estimates of product sales and distribution for use in the four major food-producing categories of animal species (cattle, swine, chickens, turkeys) will be important in supporting efforts such as NARMS, a surveillance program that monitors trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals. NARMS retail meat and animal sampling focus on the same four major food-producing species included in § 514.87(c). NARMS does not currently have a surveillance system for antimicrobial resistance pathogens

from aquaculture products. Since there is currently limited resistance data related to minor food-producing animals (including fish) and companion animals, requiring estimates of these additional species at this time would cause additional burden without clear benefit to our understanding of antimicrobial resistance. NARMS does collect some resistance data on import isolates of Salmonella, which include some seafood isolates; however, because these data are from imports, data on domestic distribution and sales of antimicrobials for use in aquaculture would not be informative to NARMS and our overall efforts to assess antimicrobial use and resistance domestically.

(Comment 11) One comment suggests that we modify proposed § 514.87(c) to remove the category “other species/unknown” and replace it with two categories, “other species” and “unknown”, so that those estimates could be independently reported.

(Response 11) We appreciate the suggestion to collect sales data on both “other species” and “unknown”; however, we have determined that there is not a clear benefit to having this information reported separately at this time. As noted in our response to comment 1, one of the reasons we believe that having species-specific estimates of product sales and distribution in the four major food-producing categories of animal species (cattle, swine, chickens, turkeys) will be important is to support data we obtain from NARMS. NARMS retail meat and animal sampling focus on the same four major food-producing species. The category “other species/unknown” will be used to capture the percentage of each new animal drug product that was sold or distributed for use in animal species other than the four major food-producing species or otherwise unknown to the reporting drug sponsor. Since there is currently limited resistance data related to minor food-producing animals and companion animals, requiring estimates of these additional species would cause additional burden without clear benefit.

(Comment 12) One comment suggests that we should not report species-specific information in our annual reports, arguing that by doing so we would disclose confidential commercial information in violation of proposed § 514.87(e).

(Response 12) As discussed in our response to comment 9, we have carefully considered the issues regarding the protection of confidential commercial information and the disclosure of species-specific information in our annual summary reports. After considering the comments received in response to the proposed rule, we are not persuaded that reporting species-specific information in our annual summary reports will lead to the disclosure of confidential commercial information. We will only provide sales data in our summary reports that has been aggregated to avoid disclosing confidential commercial information. We are finalizing the rule as proposed, which includes safeguards for the protection of confidential business information related to the reporting of species-specific estimates of sales by drug sponsors, consistent with section 512(l)(3)(E) of the FD&C Act and our disclosure regulations at § 20.61.

(Comment 13) Several comments suggest we report a wider scope of information in our annual summary reports that would be required under proposed § 514.87(f). One comment suggests we should provide more detailed information on why antimicrobials are used; for example, to distinguish use for growth promotion or disease prevention from use for disease control or treatment. Another comment suggests that we should collaborate with the USDA and the CDC to develop a communication plan to explain the implications of collected data for human and animal health.

(Response 13) We appreciate the comment that we report a wider scope of information in our annual summary reports. As required by ADUFA 105, sponsors of the affected antimicrobial new animal drug products began submitting their sales and distribution data to us on an annual

basis, and we have published summary reports of such data for each calendar year beginning with 2009. Starting in 2014, we increased the amount of data provided in our annual summary reports by including “additional data tables on the importance of each drug class in human medicine, the approved routes of administration for these antimicrobials, whether these antimicrobials are available over-the-counter or require veterinary oversight, and whether the antimicrobial drug products are approved for therapeutic purposes, or both therapeutic and production purposes.” (80 FR 28863 at 28867.)

Sponsors currently are not required to report sales and distribution data broken out by the specific purpose for which these drug products are used. Many sales of antimicrobials by drug sponsors are to distributors who, in turn, may sell to other distributors or to end users (e.g., feed mills or animal producers). Thus, this type of information (i.e., how the drug product sold by the sponsor is ultimately used in a labeled species) is generally not even known by the drug sponsor. Also, as we note in our response to comment 8, reporting species-specific estimates of sales and distribution under § 514.87 is not intended to require animal drug sponsors to conduct studies of on-farm drug use practices (80 FR 28863 at 28866) (e.g., use in particular species for particular indications). Because the sales and distribution data we are collecting from drug sponsors does not include information about how the drugs were ultimately used, such data also will not be included in our annual summary reports.

As we note in our response to comments 1, 5, and 6, we recognize that data from multiple sources are needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal agriculture. We are collaborating with the USDA and the CDC to develop a plan for collecting additional on-farm data on antimicrobial use and resistance. Such data are intended to supplement existing information, including data on the quantity of

antimicrobials sold or distributed for use in food-producing animals (reported under § 514.87 as established under this final rule) and data on antimicrobial use and resistance, for example, data collected under the NAHMS and NARMS programs.

We appreciate the comment suggesting that we collaborate with the USDA and the CDC to develop a communication plan to explain the implications of collected data for human and animal health. We will also continue to work with the USDA, the CDC, and other government agencies to analyze and report on the implications of the collected data.

(Comment 14) We received several comments suggesting modifications to how we report the data that we proposed to collect. One comment suggests we should make as much of this data as possible available to the public, while protecting confidential business information. Other comments suggest we should publish monthly sales data and State- or regional-level data.

(Response 14) We plan to report aggregate data on domestic sales and distribution for the entire reporting year, but not to include separate information for each month of the reporting year. ADUFA 105 requires drug sponsors to report sales and distribution data to us broken out by month; however, antimicrobial drug products may be used at any time up to several years after distribution. As noted in the proposed rule, we consider monthly fluctuations in drug product sales to be of limited value in reflecting when products may actually be administered to animals and interpreting antimicrobial resistance trends, since much of monthly patterns are more reflective of distribution and business practices rather than of any fluctuations in use by or sales to the end user (80 FR 28863 at 28867).

Regarding the suggestion that we report State- or regional-level data, sponsors are not required to report sales and distribution data broken out by States or regions. As we note in our response to comment 13, many sales of antimicrobials by drug sponsors are to distributors who,

in turn, may sell to other distributors or to end users (e.g., feed mills or animal producers). Thus, geographic distribution of sales as detailed as State- or regional-level sales data are generally not even known by the drug sponsors. For these reasons, we decline to make the modifications to our summary reports suggested by the commenters and are finalizing the language in § 514.87(f) as proposed.

(Comment 15) Several comments ask that we adhere to the proposed deadline of December 31st of the following year for the annual reporting of sales data.

(Response 15) We plan to publish our annual summary report for each calendar year by December 31st of the following year. We note that this deadline is widely supported by advocacy groups and some animal industry groups. Adhering to this deadline would provide up-to-date data to the stakeholders and would be necessary to inform current regulatory decisions.

In addition to the comments specific to this rulemaking that we addressed previously in this preamble, we received general comments expressing views about the use of antimicrobials, antimicrobial resistance, animal health and husbandry practices, the expansion of NARMS sampling, the enhancement of on-farm collection of information, and human antimicrobial drug use. These comments express broad policy views and do not address specific points related to this rulemaking. Therefore, these general comments do not require a response.

V. Effective and Compliance Dates

This rule is effective [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Sponsors must comply with the reporting requirements in the final rule when submitting their reports covering the period of calendar year 2016.

VI. Economic Analysis of Impacts

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. We believe that this final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the final rule will impose average annualized costs that amount to less than 0.01 percent of average annual revenues on those small entities that we expect to sponsor NADAs, we have determined that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

The Economic Analysis of Impacts of the final rule performed in accordance with Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act, and the Unfunded Mandates Reform Act is available at <http://www.regulations.gov> under the docket number(s) for this final rule and at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>.

VII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the one-time and annual reporting and recordkeeping burdens. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Antimicrobial Animal Drug Distribution Reports and Recordkeeping (21 CFR part 514)--OMB Control No. 0910-0659--Revision

Description: The ADUFA 105 legislation was enacted in 2008 to address the problem of antimicrobial resistance and to help ensure that we have the necessary information to examine safety concerns related to the use of antibiotics in food-producing animals. ADUFA 105 amended section 512 of the FD&C Act to require that sponsors of approved or conditionally

approved applications for new animal drugs containing an antimicrobial active ingredient submit an annual report to us on the amount of each such ingredient in the drug that is sold or distributed for use in food-producing animals. Each report must specify: (1) The amount of each antimicrobial active ingredient by container size, strength, and dosage form; (2) quantities distributed domestically and quantities exported; and (3) a listing of the target animals, indications, and production classes that are specified on the approved label of the product. The report must cover the period of the preceding calendar year and include separate information for each month of the calendar year. This rule also includes an additional reporting provision intended to further enhance our understanding of antimicrobial animal drug sales intended for use in specific food-producing animal species. ADUFA 105 also requires us to publish annual summary reports of the data we receive. In accordance with ADUFA 105, sponsors of the affected antimicrobial new animal drug products have submitted their sales and distribution data to us, and we have published summaries of such data, for each calendar year since 2009. Collection of information on the amount of animal antimicrobials being distributed, including species-specific information, is necessary to support our ongoing efforts to encourage the judicious use of antimicrobials in food-producing animals to help ensure the continued availability of safe and effective antimicrobials for animals and humans. We intend to use these data to supplement existing information, including data collected under the NAHMS and NARMS programs. Data from multiple sources are needed to provide a comprehensive and science-based picture of antimicrobial drug use and resistance in animal agriculture.

The final rule amends our records and reports regulation in part 514 to include the following:

- Procedures relating to the submission to us of annual sales and distribution data reports by sponsors of approved or conditionally approved antimicrobial new animal drug products sold or distributed for use in food-producing animals.
- Procedures relating to the requirement that such sponsors submit species-specific estimates of product sales as a percentage of total sales.
- Procedures applicable to our preparation and publication of summary reports on an annual basis based on the sales and distribution data we receive from sponsors of approved antimicrobial new animal drug products. The final rule includes specific parameters for the content of the annual summary reports as well as provisions intended to protect confidential business information and national security, consistent with ADUFA 105 and this Agency's regulations at § 20.61.
- Provisions that give sponsors of approved or conditionally approved antimicrobial new animal drug products that are sold or distributed for use in food-producing animals the opportunity to avoid duplicative reporting of product sales and distribution data to us under part 514.

The final rule codifies in part 514 the reporting requirements established in ADUFA 105 and includes an additional reporting provision intended to enhance our understanding of new animal drug sales intended for use in specific food-producing animal species. The final rule also revises Form FDA 3744 by providing for species-specific information to be reported. Consequently FDA is revising the reporting requirements in the associated information collection. However, the final rule does not change the recordkeeping provisions already approved under OMB control number 0910-0659.

Therefore, in compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3506(c)(2)(B)), we requested public comment on the information collection provisions of the proposed rule (80 FR 28863 at 28868). We received some public comments on the information collection topics solicited in the proposed rule as addressed previously in section IV (supporting our effort to eliminate duplicative reporting, suggesting specific modifications and different approaches, questioning or supporting the utility of the information, suggesting we wait for resolution of the current legal disputes over disclosure of confidential commercial information and suggesting we provide a specific methodology for making species-specific sales estimates). However, none of the comments suggests that we modify our burden estimates.

Description of Respondents: Animal Drug Manufacturers (Sponsors).

The total annual estimated burden for this collection of information is 9,759 hours and 538 responses. This reflects a marginal increase in burden to that currently approved under OMB control number 0910-0659 resulting from the revised reporting provisions associated with the final rule. At the same time, a review of our records reflects an overall increase in respondents to the program from 26 to 27 and we have therefore adjusted our respondent numbers accordingly.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated One-Time Reporting Burden¹

| 21 CFR Section | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Average Burden per Response | Total Hours |
|--|--------------------|---------------------------------|------------------------|-----------------------------|-------------|
| 514.87(a) through (e)-- Administrative Review of the Rule: Sponsors With Active Applications | 20 | 1 | 20 | 24 | 480 |
| 514.87(a) through (e)-- Administrative Review of the Rule: Sponsors With Inactive Applications | 7 | 1 | 7 | 1 | 7 |
| 514.87(c)--Report Species-Specific Estimate of Percent of Products Distributed Domestically | 20 | 7.50 | 150 | 2 | 300 |
| Total | | | | | 787 |

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

We base our estimate of the average burden per response on our recent experience with the existing antimicrobial animal drug distribution reports program. We base our estimate of the number of affected respondents reported in tables 1 and 2 on a review of our records of sponsors with active and inactive applications, which show that in the past 3 years the number of sponsors have increased from 26 to 27.

Table 1 shows the estimated one-time burden associated with the new reporting provisions of this final rule. We expect that current sponsors of approved or conditionally approved applications for antimicrobial new animal drugs sold or distributed for use in food-producing animals will need to review the provisions of the final rule and develop a compliance plan. Based on our records, we estimate there are a total of 27 sponsors, where 20 sponsors hold active (i.e., currently marketed) applications and 7 sponsors hold only inactive applications, as reflected in rows 1 and 2. We estimate that the 20 sponsors with active applications will take 24 hours to complete the review and develop a compliance plan. We expect that the seven sponsors with inactive applications will take 1 hour to complete the review and will not need to develop a compliance plan.

We also estimate that the 20 sponsors with 150 applications will each spend approximately 2 hours to discuss and settle upon a method to calculate the species-specific information required under § 514.87(c). This estimate is reflected in row 3.

Table 2.--Estimated Annual Reporting Burden¹

| 21 CFR Section | FDA Form | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Average Burden per Response | Total Hours |
|--|----------|--------------------|---------------------------------|------------------------|-----------------------------|-------------|
| 514.87(a) through (e)-- Annual Reports for Sponsors With Active Applications--Paper Submission | 3744 | 10 | 7.5 | 75 | 62 | 4,650 |

| 21 CFR Section | FDA Form | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Average Burden per Response | Total Hours |
|--|----------|--------------------|---------------------------------|------------------------|-----------------------------|-------------|
| 514.87(a) through (e)-- Annual Reports for Sponsors With Active Applications--Electronic Submission | 3744 | 10 | 7.5 | 75 | 52 | 3,900 |
| 514.87(a) through (e)-- Annual Reports for Sponsors With Inactive Applications--Paper Submission | 3744 | 4 | 26.5 | 106 | 2 | 212 |
| 514.87(a) through (e)-- Annual Reports for Sponsors With Inactive Applications--Electronic Submission | 3744 | 3 | 35 | 105 | 2 | 210 |
| Total | | | | | | 8,972 |

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 2 shows the estimated recurring annual reporting burden associated with the final rule. While we expect new § 514.87(c) will require 3 burden hours resulting from including species-specific estimates, we believe 1 hour will be saved by eliminating the requirement for sponsors to calculate the amount of antimicrobial active ingredients associated with their monthly product sales and distribution data (§ 514.80(b)(4)(i)(A)). Consequently, we estimate that the 20 sponsors with active applications will each expend approximately 2 additional reporting hours annually for new § 514.87. Because the Agency, upon implementation of the rule, will accept both paper and electronic submissions, and we assume that half of the respondents will report electronically, we estimate 10 respondents for each submission method as shown in rows 1 and 2.

While we estimate no increase in burden for the seven sponsors of inactive applications, we similarly will accept both paper and electronic submissions. Accordingly we have reported, unchanged, the 2 hours of burden already approved under OMB control number 0910-0659 in rows 3 and 4.

This final rule also refers to other currently approved collections of information found in our regulations. These collections of information are subject to review by OMB under the Paperwork Reduction Act of 1995. The collections of information in § 514.80 are approved under OMB control number 0910-0284. The collections of information in 21 CFR 211.196 are approved under OMB control number 0910-0139.

The information collection provisions of this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995. Prior to the effective date of this final rule, FDA will publish a notice in the Federal Register announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

IX. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

X. References

The following references are on display in the Division of Dockets Management (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m. Monday through Friday; they are also available electronically at <http://www.regulations.gov>.

FDA has verified the Web site addresses, as of the date this document publishes in the Federal Register, but Web sites are subject to change over time.

1. USDA, "Livestock & Meat Domestic Data," <http://www.ers.usda.gov/data-products/livestock-meat-domestic-data>.
2. "Food Fish Production and Sales by Species, by Size Category, by State and United States: 2005," http://www.agcensus.usda.gov/Publications/2002/Aquaculture/aquacen2005_08.pdf.
3. Painter, J. A., R. M. Hoekstra, T. Ayers, et al., "Attribution of Foodborne Illnesses, Hospitalizations, and Deaths to Food Commodities by Using Outbreak Data, United States, 1998-2008," Emerging Infectious Diseases, 19(3):407-415, 2013.
4. Gould, L. H., K. A. Walsh, A. R. Vieira, et al., "Surveillance for Foodborne Disease Outbreaks--United States, 1998-2008," Morbidity and Mortality Weekly Report. Surveillance Summaries, 62(2):1-34, 2013.
5. "Aquaculture in the United States," http://www.nmfs.noaa.gov/aquaculture/aquaculture_in_us.html.

List of Subjects in 21 CFR Part 514

Administrative practice and procedure, Animal drugs, Confidential business information, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 514 is amended as follows:

PART 514--NEW ANIMAL DRUG APPLICATIONS

1. The authority citation for part 514 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 354, 356a, 360b, 360ccc, 371, 379e, 381.

2. In § 514.80, revise the fifth sentence of paragraph (b)(4) introductory text and paragraph (b)(4)(i) to read as follows:

§ 514.80 Records and reports concerning experience with approved new animal drugs.

* * * * *

(b)* * *

(4) * * *The yearly periodic drug experience reports must be submitted within 90 days of the anniversary date of the approval of the NADA or ANADA. * * *

(i) Distribution data. (A) Information about the distribution of each new animal drug product, including information on any distributor-labeled product. This information must include the total number of distributed units of each size, strength, or potency (e.g., 100,000 bottles of 100 5-milligram tablets; 50,000 10-milliliter vials of 5-percent solution). This information must be presented in two categories: Quantities distributed domestically and quantities exported.

(B) Applicants submitting annual sales and distribution reports for antimicrobial new animal drug products under § 514.87 have the option not to report distribution data under paragraph (b)(4)(i)(A) of this section for the approved applications that include these same products, but only provided each of the following conditions are met:

(1) Applicants must have submitted complete periodic drug experience reports under this section for such applications for at least 2 full years after the date of their initial approval.

(2) Applicants must ensure that the beginning of the reporting period for the annual periodic drug experience reports for such applications is January 1. For applications that currently have a reporting period that begins on a date other than January 1, applicants must

request a change in reporting submission date such that the reporting period begins on January 1 and ends on December 31, as described in paragraph (b)(4) of this section.

(3) Applicants that change their reporting submission date must also submit a special drug experience report, as described in paragraph (b)(5)(i) of this section, that addresses any gaps in distribution data caused by the change in date of submission.

(4) Applicants who choose not to report under paragraph (b)(4)(i)(A) of this section must ensure that full sales and distribution data for each product approved under such applications are alternatively reported under § 514.87, including products that are labeled for use only in nonfood-producing animals.

* * * * *

3. Add § 514.87 to subpart B to read as follows:

§ 514.87 Annual reports for antimicrobial animal drug sales and distribution.

(a) The applicant for each new animal drug product approved under section 512 of the Federal Food, Drug, and Cosmetic Act, or conditionally approved under section 571 of the Federal Food, Drug, and Cosmetic Act, and containing an antimicrobial active ingredient, must submit an annual report to FDA on the amount of each such antimicrobial active ingredient in the drug that is sold or distributed in the reporting year for use in food-producing animal species, including information on any distributor-labeled product.

(b) This report must identify the approved or conditionally approved application and must include the following information for each new animal drug product described in paragraph (a) of this section:

(1) A listing of each antimicrobial active ingredient contained in the product;

(2) A description of each product sold or distributed by unit, including the container size, strength, and dosage form of such product units;

(3) For each such product, a listing of the target animal species, indications, and production classes that are specified on the approved label;

(4) For each such product, the number of units sold or distributed in the United States (i.e., domestic sales) for each month of the reporting year; and

(5) For each such product, the number of units sold or distributed outside the United States (i.e., quantities exported) for each month of the reporting year.

(c) Each report must also provide a species-specific estimate of the percentage of each product described in paragraph (b)(2) of this section that was sold or distributed domestically in the reporting year for use in any of the following animal species categories, but only for such species that appear on the approved label: Cattle, swine, chickens, turkeys. The total of the species-specific percentages reported for each product must account for 100 percent of its sales and distribution; therefore, a fifth category of “other species/unknown” must also be reported.

(d) Each report must:

(1) Be submitted not later than March 31 each year;

(2) Cover the period of the preceding calendar year; and

(3) Be submitted using Form FDA 3744, “Antimicrobial Animal Drug Distribution Report.”

(e) Sales and distribution data and information reported under this section will be considered to fall within the exemption for confidential commercial information established in § 20.61 of this chapter and will not be publicly disclosed, except that summary reports of such information aggregated in such a way that does not reveal information that is not available for

public disclosure under this provision will be prepared by FDA and made available to the public as provided in paragraph (f) of this section.

(f) FDA will publish an annual summary report of the data and information it receives under this section for each calendar year by December 31 of the following year. Such annual reports must include a summary of sales and distribution data and information by antimicrobial drug class and may include additional summary data and information as determined by FDA. In order to protect confidential commercial information, each individual datum appearing in the summary report must:

(1) Reflect combined product sales and distribution data and information obtained from three or more distinct sponsors of approved products that were actively sold or distributed that reporting year, and

(2) Be reported in a manner consistent with protecting both national security and confidential commercial information.

Dated: May 6, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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