U.S. Food & Drug Administration
Animal Drug Adverse Event Reporting and Recordkeeping

OMB Control No. 0910-0284; Revision

SUPPORTING STATEMENT **Part A: Justification**

Terms of Clearance: *Approved with the understanding that FDA is currently seeking public comment on this collection and revisions may be made to the new electronic submission instrument as part of the upcoming extension request.*

In accordance with these terms, FDA has published both a 60- and 30-day notice in the Federal Register specifically inviting public comment on the proposed collection instruments. This is discussed more fully under ***Question 8*** below. FDA also notes that current rulemaking is underway (RIN 0910-AH51) to revise the underlying regulations associated with the information collection. The rule does not change the content of the postmarketing reports already covered, but rather, proposes to require that certain submissions be made in an electronic form. At the same time, the rule also proposes a provision for temporary waiver of the requirement and establishes procedures for respondents to request such a waiver. We believe electronic submissions facilitate agency review of adverse experiences associated with animal drugs and ultimately impose minimal burden on respondents to the information collection.

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA) regulations. With regard to adverse events and product/manufacturing defects associated with approved new animal drugs, section 512(l) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360b(l)) requires applicants with approved new animal drug applications (NADAs) and abbreviated new animal drug applications (ANADAs) to establish and maintain records and reports of data relating to experience with uses of such drug, or with respect to animal feeds bearing or containing such drug, to facilitate a determination under section 512(e) as to whether there may be grounds for suspending or withdrawing approval of the NADA or ANADA under section 512(e) or 512(m)(4).

Sections 571(e)(3) and 512(e)(2) of the FD&C Act (21 U.S.C. 360ccc(e)(3) and 360b(e)(2)) require that applicants with conditionally approved new animal drug applications (CNADAs) maintain adequate records and make reports in accordance with a regulation or order issued under section 512(l). Section 512(m)(5) of the FD&C Act requires an applicant for a license to manufacture animal feeds bearing or containing new animal drugs to maintain adequate records and make reports "*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*" whether there may be grounds for suspending or withdrawing approval of the new animal drug under section 512(e) or a license to manufacture animal feeds bearing or containing new animal drugs under section 512(m)(4).

Finally, section 514.80 of our regulations (21 CFR 514.80) sets forth recordkeeping and reporting requirements for applicants and nonapplicants of approved NADAs and ANADAs. FDA revised its burden tables at Question 12 below to more clearly reflect that provisions associated with section 510.301 of our regulations (21 CFR 510.301), setting forth recordkeeping and reporting requirements for licensed medicated feed manufacturing facilities, are included in this information collection. Specifically, individual rows were added to reflect burden for activities associated with this particular requirement.

To assist respondents with the reporting provisions required by the regulations, we have developed the following forms:

Forms FDA 1932 and 1932a – "*Veterinary Adverse Drug Reaction, Lack of Effectiveness, Product Defect Report"* (paper-based and e-form); Forms FDA 2301 – "*Transmittal of Periodic Reports and Promotional Material New Animal Drugs"*; and Form FDA 3744 (e-form using eSubmitter "*Antimicrobial Animal Drug Distribution Report*." Minor editorial revisions to Form FDA 1932a clarify how to report adverse drug events associated with compounded products using that form. Respondents already report adverse drug events associated with compounded products using Form FDA 1932a. The clarifications include the addition of a new question, "*Is this a compounded product*"; the addition of a new field to allow the submitter to provide product strength, "*Strength of Active Ingredient(s)*"; modifying the title of the existing field requesting the name of manufacturer, so that it reads, "*Name of Manufacturer or Compounding Pharmacy/Compounder of Suspected Product*"; and a request for contact information for the manufacturer or compounder.

We therefore request extension of OMB approval for the information collection provisions found in the applicable regulations under 21 CFR Part 510 and 514 and the supporting collection instruments.

2. Purpose and Use of the Information Collection

The information collection allows FDA to implement specified public health protection provisions under the FD&C Act regarding approved new animal drugs. Respondents are those submitting adverse experience reports consistent with the applicable laws and regulations.

3. Use of Improved Information Technology and Burden Reduction

Many of the applicants have automated systems for reports of adverse drug experiences to new animal drugs. Under 21 CFR 514.80(d) applicants may electronically generate Form FDA 1932 or Form FDA 2301. CVM works domestically with the animal pharmaceutical industry and internationally under VICH to develop methods and standards for electronic submission. Form FDA 1932 and Form FDA 1932 may be electronically submitted via the FDA Safety Reporting Portal. Form FDA 2301 may be electronically submitted to the agency via eSubmitter. Burden for the electronic version of Forms FDA 1932 and 1932a is accounted for under OMB control number 0910-0645. FDA anticipates over time that adverse event reporting for small businesses will shift more and more to the electronic FDA Safety Reporting Portal. We estimate that 95%

of the respondents will use electronic means to fulfill the agency's requirement or request in the next three years.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information. Electronic adverse event reporting for approved new animal drugs (including mandatory reporting under § 514.80(b) and voluntary reporting) has been approved under OMB control number 0910-0645. Reporting and recordkeeping associated with the index of legally marketed unapproved new animal drugs for minor species (21 CFR part 516) is approved under OMB control number 0910-0620.

5. Impact on Small Businesses or Other Small Entities

Although new animal drug development is typically an activity completed by large drug firms, the information collection required under 21 CFR 510.301 and 21 CFR 514.80 applies to all respondents. However, FDA aids small businesses in complying with its requirements through Regional Small Business Representatives and scientific and administrative staffs within the agency. Also, a Small Business Guide is available on our website at: www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm.

We estimate that 10% of the respondents are small businesses.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory requirements and requires reporting on only an occasional basis. Regulations at 21 CFR 510.301 and 21 CFR 514.80 establish a reporting frequency underscoring the need to focus on potential problems concerning the safety and effectiveness of new animal drugs. Less frequent collection hinders early detection of public health threats intended to be covered by the regulations.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The reporting requirements under 21 CFR 510.301(a) and (b), 21 CFR 514.80(b)(1), (b)(2)(i)-(ii), (b)(3), and (e) are inconsistent with 5 CFR 1320.5. This section requires justification for requesting respondents to report more often than quarterly. Under 21 CFR 510.301(a) and (b), a licensed medicated feed manufacturer must submit certain information to us immediately and other information to us within 15 days. Pursuant to 21 CFR 514.80(b)(1), the applicant is required to submit product and manufacturing defects that may result in serious adverse drug events within 3 working days of first becoming aware that a defect may exist. Pursuant to 21 CFR 514.80(b)(2)(i)-(ii), the applicant is required to submit initial and follow-up reports within 15 working days. Pursuant to 21 CFR 514.80(b)(3), the non-applicant required to report adverse drug experiences to the applicant within 3 working days of first receiving the information or if reported to FDA within 15 working days. This shorter reporting time is necessary to inform FDA as soon as possible of serious problems associated with a regulated product so that appropriate action may be taken to offset threats to the public health.

The maintenance period for keeping records is also inconsistent with 5 CFR 1320.6. Pursuant to 21 CFR 514.80(e), the applicant and non-applicant must maintain records and reports of all information for a period of 5 years after the date of submission. This extended period is due to the potential for litigation, delayed recognition of adverse drug experiences, long expiration dates, and needed for studies of delayed effects such as carcinogenicity.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice in the Federal Register of July 18, 2017 (82 FR 32829) inviting public comment for the information collection. In the notice we specifically invited feedback regarding FDA reporting forms and have made revisions as discussed previously in this supporting statement. At the same time, we made no other revisions. We therefore retain our burden estimate but note that FDA remains open to improving its forms and continually welcomes feedback including suggested revisions that might assist respondents with the information collection.

9. Explanation of Any Payment or Gift to Respondents

There are no payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

During working hours, only FDA employees have access to the computer files and database on a need to know basis. During duty and non-duty hours building security is provided through a contract with a private protection agency. None of the provisions bar the release of the confidential information if subpoenaed by a court of law. Confidentiality of the information submitted under these reporting requirements is protected under 21 CFR 514.11 and under 21 CFR part 20. The unauthorized use of disclosure of the trade secrets required in applications is specifically prohibited under the Section 310(j) of the Act. Further, under the terms of the Freedom of Information Act, the veterinarian's name, address, and phone number, and the owner's name, etc., reported on Form FDA 1932 cannot be made available to a public request.

11. Justification for Sensitive Questions

This information does not contain questions pertaining to sex behavior, attitude, religious beliefs, or any other matter commonly considered private or of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

Description of respondents: Respondents to this collection of information are animal drug manufacturers with approved NADAs, ANADAs, or CNADAs, as well as licensed commercial feed mills and licensed mixer-feeders.

Information collection provisions found in the regulations include:

21 CFR 510.301 – Recordkeeping; requires a licensed medicated feed manufacturer to keep records concerning any mixup in the new animal drug or its labeling; any bacterial or significant chemical, physical, or other change or deterioration in a drug; any failure of one or more distributed batches of a drug to meet the specifications established for it; any unexpected side effect, injury, toxicity, or sensitivity reaction or any unexpected incidence or severity thereof, and any unusual failure of the new animal drug to exhibit its expected pharmacological activity.

21 CFR 514.80(e) – Recordkeeping; requires maintenance of records and files containing full records of information pertinent to the safety or effectiveness of a new animal drug for a period of 5 years after the date of submission.

21 CFR 510.301(a) and (b) – Reporting; requires a licensed medicated feed manufacturer to immediately report to us information concerning any mixup in the new animal drug or its labeling; any bacterial or significant chemical, physical, or other change or deterioration in a drug; and any failure of one or more distributed batches of a drug to meet the specifications established for it. A licensed medicated feed manufacturer must report to us within 15 working days of receipt of information concerning any unexpected side effect, injury, toxicity, or sensitivity reaction or any unexpected incidence or severity thereof, and any unusual failure of the new animal drug to exhibit its expected pharmacological activity.

21 CFR 514.80(b)(1) – Reporting; specifies information pertaining to product defect/manufacturing defects that may result in serious adverse drug events is to be reported within 3 working days of first becoming aware that a defect may exist.

21 CFR 514.80(b)(2)(i) – Reporting; specifies requirement that initial reports of serious adverse drug events and unexpected adverse drug events are to be submitted within 15 working days of first receiving the information.

21 CFR 514.80(b)(2)(ii) – Reporting; specifies requirements for submitting follow-up reports to the initial report of serious adverse drug events and unexpected adverse drug events.

21 CFR 514.80(b)(3) – Reporting; specifies requirements by nonapplicants to forward reports of adverse drug events to the applicant within 3 working days of first receiving the information. Nonapplicants may also elect to submit reports directly to FDA within 15 working days of first receiving the information.

21 CFR 514.80(b)(4)(i)-(iv) – Reporting; specifies requirements for submitting 6 month periodic drug experience reports for the first two years following approval and then yearly thereafter. Specifies for yearly drug experience reports that applicants may petition FDA to change the date of reporting and(or) the frequency of reporting. Specifies requirements for submitting distribution data for each new animal drug product for quantities distributed domestically and quantities exported; applicant and distributor current package labeling; nonclinical laboratory studies and clinical data not previously submitted; and adverse drug experiences not previously submitted.

21 CFR 514.80(b)(5)(i) – Reporting; specifies requirements for submitting special drug experience reports at different times or more frequently from those stated in 21 CFR 514.80.

21 CFR 514.80(b)(5)(ii) – Reporting; specifies requirements for submitting advertisements and promotional labeling.

21 CFR 514.80(b)(5)(iii) – Reporting; specifies requirements for submitting distributor statements.

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

12 a. Annualized Hour Burden Estimate

Table 1 – Estimated Annual Reporting Burden[1]

21 CFR Part and/or Activity	FDA Form	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
Medicated feed reports; §510.301(a) and (b)	N/A	5	1	5	.25 (15 minutes)	1.25
Mandatory adverse event reporting; 21 U.S.C. 360b(l); §514.80(b)(1); (b)(2)(i) and (ii); (b)(3); and (b)(4)(iv)(A)	1932	22	81	1,782	1	1,782
Voluntary adverse event reporting by veterinarians and the general public	1932a	197	1	197	1	197
Periodic drug experience reports; §514.80(b)(4)	2301	200	8.11	1,622	16	25,952
Special drug experience reports; §514.80(b)(5)(i)	2301	200	0.57	117	2	228
Submission of advertisements and promotional labeling; §514.80(b)(5)(ii)	2301	200	20.12	4,024	2	8,048
Submission of distributor statements, §514.80(b)(5)(iii)	2301	190	0.1	19	2	38
Total						36,246.25

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

Table 2 – Estimated Annual Recordkeeping Burden[1]

21 CFR Part and Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Recordkeeping; §510.301[2]	5	1	5	4	20
Recordkeeping; 21 U.S.C. 360b(l) and §514.80(e)[3]	646.70	7.19	4,649.8	14	65,097
Total					65,117

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.
[2]This estimate includes all recordkeeping by licensed medicated feed manufacturers under §510.301.
[3]This estimate includes all recordkeeping by applicants of approved NADAs, ANADAs, and CNADAs under §514.80(e).

We base our reporting and recordkeeping estimates on our experience with adverse event reporting for approved new animal drugs and the number of reports received in the previous 3 years. Included in our estimate is recordkeeping burden for medicated feed adverse event reports as part of our estimate of the recordkeeping burden of all mandatory adverse event reports for new animal drugs. To improve the clarity of our estimates we have added a row to table 2, on which we separately report our recordkeeping estimate for medicated feed adverse event reports (20 hours).

12b. Annualized Cost Burden Estimate

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Industry Compliance Officer	101,363	$47.60	$4,825,487

[1] May 2016 National Industry-Specific Occupational Employment and Wage Estimates, Bureau of Labor Statistics and including 30% for benefits (https://www.bls.gov/oes/current/naics4_325400.htm).

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

Costs to the Federal Government are absorbed through existing resource allocations.

15. Explanation for Program Changes or Adjustments

We characterized this request as a revision to clarify that provisions under 21 CFR 510.301 are included in the collection. We revised the burden tables at Q.12 of this supporting statement accordingly. Also, and as discussed previously in this supporting statement and in our Federal Register notices, we made minor editorial revisions to the paper and electronic versions of Form FDA 1932a to clarify how to report adverse drug events associated with compounded products. We also made adjustments. Specifically, the collection reflects a nominal increase in the estimated number of submissions by 7.8 responses consistent with our review of the collection. At the same time, there is a 1.75 decrease in burden hours that we attribute to improvements in the reporting instruments.

16. Plans for Tabulation and Publication and Project Time Schedule

Information is not to be published for statistical use.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

Display of the OMB Expiration Date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.