The Office of the Chief Information Officer is responsible for providing centralized information technology (IT) policy, procedures, standards, and guidelines. OCIO’s responsibilities include: Strategy, policy and IT governance, including performance measurement and innovation; security, privacy, and risk management, including business continuity, standardization and oversight of business processes, external compliance, and security strategy and management; financial and vendor management and IT acquisition oversight, including acquisition strategies, technological approaches, performance measurement, vendor selection, cost estimating and optimization; service planning and architecture, including quality management and enterprise architecture; program and project management; portfolio management, applications management, development, and maintenance; IT infrastructure and operations; and data services, big data analytics and business intelligence.

The Division of Portfolio Management & Governance provides centralized IT portfolio management functions to include: IT governance execution services, vendor management services, IT process training services, IT acquisition oversight, portfolio risk management, portfolio performance metrics reporting and analysis, post-award acquisition support, enterprise architecture compliance oversight, 508 Compliance oversight, finance and budget execution services, integration services, and independent verification testing services.

The Division of Policy, Strategy, and Planning is responsible for providing governance and oversight of centralized enterprise wide IT functions across ACF which includes: Strategy, policy and IT governance, IT planning and strategic goal alignment, enterprise architecture definition and oversight, pre-award acquisition support, IT budget definition and oversight, Capital Planning and Investment Control (CPIC) services, and business relationship management and IT investment planning services.

The Division of Cyber Security & Privacy provides overall IT Security Management for all ACF systems including security and privacy risk management, security architecture and engineering support services, security assessments and authorizations, privacy and security incident response services, privacy impact assessments, vulnerability management, security operations functions, security testing, and security and privacy policy and governance.

The Division of Service & Solution Delivery provides overall solution delivery and operations services, including: Project management, application development, quality assurance testing services, infrastructure and operations maintenance services, system/application training services, data processing services and overall customer support service delivery services, i.e. service desk operations.


Steven Wagner,
Acting Assistant Secretary for Children and Families.

[FR Doc. 2018–11125 Filed 5–23–18; 8:45 am]
BILLING CODE 4184–40–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–1558]

Food and Drug Administration’s Evaluation of Approaches To Demonstrate Effectiveness of Heartworm Preventatives for Dogs; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA or we) is evaluating its current thinking regarding the design of studies intended to generate data to support substantial evidence of effectiveness for investigational new animal drugs intended for the prevention of heartworm disease in dogs. We are specifically requesting public input on possible alternative approaches for evaluating such products or information to assist in the potential development of alternative recommended study designs.

DATES: Submit either electronic or written comments on the proposed method by August 22, 2018.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before August 22, 2018. The https://www.regulations.gov electronic filing system will accept comments until midnight Eastern Time at the end of August 22, 2018. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for confidential business information, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”)
Instructions: All submissions received must include the Docket No. FDA–2018–N–1558 for “FDA’s Evaluation of Approaches to Demonstrate Effectiveness of Heartworm Preventatives for Dogs.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.fda.gov/regulatoryinformation/dockets/default.htm.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the proposed method to the Policy and Regulations Staff (HFV–6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. Persons with access to the internet may obtain the draft guidance at either https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052417.pdf or https://www.regulations.gov.

FOR FURTHER INFORMATION CONTACT:
Steven Fleischer, Center for Veterinary Medicine (HFV–110), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240–402–0809, steven.fleischer@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: FDA is evaluating its current thinking regarding the design of studies intended to generate data to support substantial evidence of effectiveness for investigational new animal drugs intended for the prevention of heartworm disease in dogs.

An application for a new animal drug shall include “evidence to establish safety and effectiveness” (21 CFR 514.1(b)(8)). Additionally, “an application may be refused unless it includes substantial evidence of the effectiveness of the new animal drug as defined in 514.4 [21 CFR 514.4]” (21 CFR 514.1(b)(8)(ii)). Regarding studies, under 21 CFR 514.4(b)(3)(i) substantial evidence of the effectiveness of a new animal drug for each intended use and associated conditions of use shall consist of a sufficient number of current adequate and well-controlled studies of sufficient quality and persuasiveness to permit qualified experts:

- To determine that the parameters selected for measurement and the measured responses reliably reflect the effectiveness of the new animal drug;
- To determine that the results obtained are likely to be repeatable, and that valid inferences can be drawn to the target animal population [(independent substantiation and inferential value)]; and
- To conclude that the new animal drug is effective for the intended use at the dose or dose range and associated conditions of use prescribed, recommended, or suggested in the proposed labeling.

The current recommended approach to demonstrating substantial evidence of effectiveness of an investigational new animal drug intended for the prevention of heartworm disease is for sponsors to conduct two laboratory dose confirmation studies and one multi-site field safety and effectiveness study under the principles of Good Clinical Practice (GCP) as described in Guidance for Industry #85, “Good Clinical Practice (VICH GL9).”1 The laboratory dose confirmation studies are experimentally-induced infection studies, each conducted at different laboratory facilities, led by independent investigators and using recent isolates of Dirofilaria immitis from two separate United States geographic locations. The field effectiveness study is a multi-site study conducted with investigators in various geographical regions of the continental United States with endemic heartworm disease that evaluates the use of the investigational new animal drug in client-owned animals.

Both study types have strengths and limitations. Strengths of the laboratory studies include the use of a negative control group, which provides direct evidence of the effect of the new animal drug and that results are not due to the impact of other treatments or external influences on disease transmission and progression. In addition, laboratory studies allow for appropriate classification of exposure due to contemporaneous experimental infection of the same number of infectious D. immitis larvae to control and investigational new animal drug-administered groups and the appropriate classification of outcome due to performance of an adult worm count post mortem. The worm count allows for qualitative and quantitative evaluation of outcome by determining the presence of adult worms as well as the determination of the individual worm burden in each dog. One significant limitation of the laboratory studies is the evaluation of only two isolates. Although each isolate should be from a different geographic area in the United States, under laboratory conditions the isolates may not accurately represent the current diversity of D. immitis in the United States and may not account for variable susceptibility in the isolates in the field. From a substantial evidence of effectiveness standpoint, this condition limits the inferential value of the two studies because the use of the laboratory isolates may over- or under-represent the relative susceptibility of other isolates in the field to the investigational new animal drug.

Additionally, the small number of animals used in the study limits confidence in the interpretation of effectiveness results.

The strength of the field study is that the study evaluates the investigational new animal drug under actual conditions of use and with the current

endpoint.

Standard. To address these gaps, we are
interested in evaluating alternative
preventatives for use in dogs, we are
during the critical first few months of
the study is lacking, which complicates
interpretation of a negative antigen test
at the end of the study. If the study is
started during a time of low
transmission, such as in winter,
exposure is even more uncertain.
Because of the delay in the ability to
detect an adult heartworm infection, it
is impossible to tell with certainty if
infections detected between 4 and 8
months after study initiation were pre-
existing infections or due to lack of
effectiveness of the preventative.
Obtaining false negative and false
positive antigen test results are possible
and, because worm counts are not
performed, the false results may result
in the misclassification of outcome for
individual dogs.

In recognition of the limitations of the
current recommended laboratory and
field effectiveness studies for heartworm
preventatives for use in dogs, we are
interested in evaluating alternative
approaches to these study designs that
would mitigate the limitations of such
studies while ensuring that the studies
generate data to support substantial
 Evidence of effectiveness as defined in
21 CFR 514.4.

Currently, there are gaps in
knowledge and understanding that
prevent us from fully evaluating
alternative approaches to meeting the
substantial evidence of effectiveness
standard. To address these gaps, we are
seeking public comment regarding the
following questions:

Population level effectiveness
endpoint. The design and evaluation of
effectiveness studies rely on an
understanding of the appropriate
outcome measure. In seeking to design
alternative study approaches, we would
like to determine a population level
effectiveness endpoint that could be
used to design future studies. Currently
we do not have a defined level of
performance that heartworm
preventatives are expected to meet
when applied to the entire United States
canine population. Determining a
population level endpoint would allow
us to explore the suitability and
feasibility of alternative study designs
for the evaluation of effectiveness for
heartworm preventatives. Factors that
may contribute to a heartworm
preventative’s effectiveness include the
inherent potency of the drug,
differences in heartworm susceptibility,
and owner compliance.

1. Assuming that a product was
administered according to labeled
directions, what would be an
acceptable rate of failure of an
approved heartworm preventative in
the overall United States
canine population to which it is
administered?

2. What would be the maximum
acceptable rate of failure in a
high-risk population?

3. Alternatively, if you do not have
a numerical estimate, what
recommendations do you have for
determining what an acceptable rate of
failure should be?

Exposure to infective D. immitis
larvae. For humane reasons, field
studies are not conducted with a
negative control group that would
reflect the study population’s level
of exposure to heartworm infection.
Therefore, it is necessary to have other
measures to ensure that the level of
exposure to infective D. immitis
larvae experienced in the study is
sufficient to adequately test the
effectiveness of the investigational
new animal drug. Please
provide comment on other methods
that could reliably be used to ensure
adequate exposure of dogs enrolled in
a field study. Consider the following
points:

4. Can available tests be used to
determine an individual dog’s
exposure to infective larvae? What are
the sensitivity and specificity of those
tests in this application? How would
the level of sensitivity and specificity of
these tests impact the reliable
assessment of rate of failure in the
population?

5. Does the use of a heartworm
preventative, even if only partially
effective, have an impact on the results
of these tests?

6. Could methods that consider a
wider area (as opposed to an
individual animal) such as mosquito
testing, forecasting, or modeling be
reliably used to determine the likely
exposure to infective larvae of
dogs at a specific study site? What
information would be needed to create
the methods or to verify the validity of
the methods? What are the
limitations to such an approach?

Outcome Assessment. Accurate
assessment of the outcome endpoint
(heartworm infection) is essential for
field studies where necropsy worm
counts will not be performed.

7. What are the most reliable ways
of properly classifying the outcome in
a non-terminal study?

8. Are there critical pieces of
information supporting substantial
evidence of effectiveness that can only
be gained from a well-controlled
laboratory study? Are there elements
that could be added to a field study that
would partially address those data gaps?

Other.

9. Are there laboratory study
designs other than the traditional dose
confirmation study that provide
additional information or include a
model that is more representative of real
world exposure? For example, the use of
live mosquitoes to induce infection
rather than the mechanical injection
of larvae.

10. How might differences in the
route of administration, dosing
frequency, or pharmacokinetic factors
impact effectiveness? How might
studies be designed to incorporate these
factors? For example, a drug that
demonstrates an early peak, with
minimal to no drug levels in the dog
for the remainder of the dosing interval
versus a product with continuous
drug levels in the dog for the entire
dosing interval?

Dated: May 21, 2018.

Leslie Kux,
Associate Commissioner for Policy.

[FR Doc. 2018–11132 Filed 5–23–18; 8:45 am]
BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND
HUMAN SERVICES

Food and Drug Administration


Agency Information Collection
Activities; Proposed Collection;
Comment Request; Current Good
Manufacturing Practice, Hazard
Analysis, and Risk-Based Preventive
Controls for Food for Animals

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is
announcing an opportunity for public
comment on the proposed collection of
certain information by the Agency.

Under the Paperwork Reduction Act of
1995 (PRA), Federal Agencies are
required to publish notice in the
Federal Register concerning each
proposed collection of information,