Food and Drug Administration Guidance for Industry:
Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims

OMB Control Number 0910-0670

SUPPORTING STATEMENT

Terms of Clearance: None

A. **Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA or we) guidance regarding the labeling of drugs that include a hypertension indication. FDA has issued a guidance document for industry entitled, "*Guidance for Industry(GFI): Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims,"* that is intended to assist respondents in developing labeling for outcome claims for drugs that are indicated to treat hypertension. With few exceptions, current labeling for antihypertensive drugs includes only the information that these drugs are indicated to reduce blood pressure; the labeling does not include information on the clinical benefits related to cardiovascular outcomes expected from such blood pressure reduction. However, blood pressure control is well established as beneficial in preventing serious cardiovascular events, and inadequate treatment of hypertension is acknowledged as a significant public health problem. FDA believes that the appropriate use of these drugs can be encouraged by making the connection between lower blood pressure and improved cardiovascular outcomes more explicit in labeling. The guidance encourages applicants to submit labeling supplements containing the new language.

2. Purpose and Use of the Information Collection

Respondents to the collection are manufacturers of antihypertensive drugs. The guidance provides non-binding recommendations intended to assist respondents in developing labeling for outcome claims for drugs that are indicated to treat hypertension. The intent of the guidance is to provide common labeling for antihypertensive drugs except where differences are clearly supported by clinical data. The guidance encourages applicants to submit labeling supplements containing the new language.

3. Use of Improved Information Technology and Burden Reduction

Although the guidance does not specifically prescribe the use of automated, electronic, mechanical, or other technological collection techniques or other forms of information technology, FDA has issued guidance documents to assist applicants in submitting information to the agency in electronic format. These guidance documents are available at FDA's website http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

The information collection applies to large and small businesses alike. FDA provides small business and industry assistance to respondents through the Center for Drug Evaluation and Research (CDER), available on FDA's website at www.fda.gov.

6. Consequences of Collecting the Information Less Frequently

There is no periodic submission of information under the guidance. Recommendations are non-binding.

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

There are no special circumstances for this collection of information.

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 soliciting public comment in the Federal Register of February 22, 2016 (81 FR 8726). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under this guidance is protected under 21 CFR 314.430 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the FD&C Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimate

We estimate the burden for the information collection as follows:

(1) Section IV.C of the guidance requests that the CLINICAL STUDIES section of the Full Prescribing Information of the labeling should include a summary of placebo- or active-controlled trials showing evidence of the specific drug's effectiveness in lowering blood pressure. If trials demonstrating cardiovascular outcome benefits exist, those trials also should be summarized in this section. Table 1 in Section V of the guidance contains the specific drugs for which the FDA has concluded that such trials exist. If there are no cardiovascular outcome data to cite, one of the following two paragraphs should appear:

> "*There are no trials of [DRUGNAME] or members of the [name of pharmacologic class] pharmacologic class demonstrating reductions in cardiovascular risk in patients with hypertension," or*
>
> *"There are no trials of [DRUGNAME] demonstrating reductions in cardiovascular risk in patients with hypertension, but at least one pharmacologically similar drug has demonstrated such benefits*."

In the latter case, the applicant's submission generally should refer to Table 1 in section V of the guidance. If the applicant believes that Table 1 is incomplete, it should submit the clinical evidence for the additional information to Docket No. FDA-2008-D-0150. The labeling submission should reference the submission to the docket. FDA estimates that no more than one submission to the docket will be made annually from one company, and that each submission will take approximately 10 hours to prepare and submit. Concerning the recommendations for the CLINICAL STUDIES section of the Full Prescribing Information of the labeling, FDA regulations at 21 CFR 201.56 and 201.57 require such labeling, and the information collection associated with these regulations is approved by OMB under OMB Control Number 0910-0572.

(2) Section VI.B of the guidance requests that the format of cardiovascular outcome claim prior approval supplements submitted to FDA under the guidance should include the following information:

1. A statement that the submission is a cardiovascular outcome claim supplement, with reference to the guidance and related Docket No. FDA-2008-D-0150.

2. Applicable FDA forms (e.g., 356h, 3397).

3. Detailed Table of Contents.

4. Revised labeling:

    a. Include draft revised labeling conforming to the requirements in 21 CFR 201.56 and 201.57;
    b. Include marked-up copy of the latest approved labeling, showing all additions and deletions, with annotations of where supporting data (if applicable) are located in the submission.

In calendar years 2014 and 2015, no submissions to Docket No. FDA-2008-D-0150 were made,

and FDA has not expended any resources in review of material related to the docket. For purposes of this information collection approval, we are estimating that we may receive one submission annually, and that each supplement will take approximately 20 hours to prepare and submit. The guidance also recommends that other labeling changes (e.g., the addition of adverse event data) should be minimized and provided in separate supplements, and that the revision of labeling to conform to §§ 201.56 and 201.57 may require substantial revision to the ADVERSE REACTIONS or other labeling sections.

(3) Section VI.C of the guidance states that applicants are encouraged to include the following statement in promotional materials for the drug.

> "*[DRUGNAME] reduces blood pressure, which reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals*."

The inclusion of this statement in the promotional materials for the drug would be exempt from OMB review based on 5 CFR 1320.3(c)(2), which states that "[t]he public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public is not included . . . ." within the definition of "collection of information."

Table 1.--Estimated Annual Reporting Burden

Activity	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Hours Per Response	Total Hours
Submission to Docket Number FDA-2008-D-0150	1	1	1	10	10
Cardiovascular Outcome Claim Supplement Submission	1	1	1	20	20
Total					30

12b. Annualized Cost Burden Estimates

FDA estimates a cost of $2,550 for industry to submit the information collection requested in this guidance.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
NDA applicants	30	$85	$2,550

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

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

14. Annualized Cost to the Federal Government

FDA medical officers will spend approximately 1 hour reviewing each cardiovascular outcome claim supplement and approximately 2 hours reviewing any clinical evidence submitted to Docket No. FDA-2008-D-0150. FDA project managers will spend about 2 hours per submission for tracking and management tasks. Based on an hourly wage rate of $70, medical review costs total $210 ($70 x 1 hour x 1 CV Outcome supplements; $70 x 2 hours x 1 submission to the Docket). Based on an hourly wage rate of $40, project management costs would total $160 ($40 x 2 hours x 2 submissions). Cumulatively this results in an annual cost of $370 to the Federal Government.

15. Explanation for Program Changes or Adjustments

As companies accomplish the objectives outlined in the guidance document, FDA expects the information collection burden to continue to diminish. In calendar years 2014 and 2015, we did not receive any reporting under **IC 1** (*submissions to Docket No. FDA-2008-D-0150*) , however, for purposes of this information collection approval, we retain our estimate that we may receive one submission annually. Under **IC 2** (*cardiovascular outcome claims*) we have adjusted our estimate to reflect **19 fewer annual responses** and **380 fewer annual burden hours** based on our experience with the collection since its last approval.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans for tabulation and publication and a project time schedule.

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

Display of OMB expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.