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 guidance is intended to assist applicants 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 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.

2. Purpose and Use of the Information Collection

The guidance is intended to assist applicants in developing labeling for outcome claims for drugs that are indicated to treat hypertension. 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.

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 web site http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

4. Efforts to Identify Duplication and Use of Similar Information

There is no duplicate information collection under this guidance.

5. Impact on Small Businesses or Other Small Entities

The guidance recommends labeling changes from all hypertension drug applicants, both large and small.

6. Consequences of Collecting the Information Less Frequently

There is no periodic submission of information under the guidance.

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 for public comment in the FEDERAL REGISTER of 04/18/2013 (78 FR 23271). 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 sensitive questions.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimate

The guidance contains two provisions that are subject to OMB review and approval under the PRA, and one provision that would be exempt from OMB review:

(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.

FDA estimates that approximately 20 cardiovascular outcome claim supplements will be submitted annually from approximately 8 different companies, 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 "The 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."

FDA requests comments on the information collection provisions described above and set forth in the following table:

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	8	2.5	20	20	400
Total					410

12b. Annualized Cost Burden Estimates

FDA estimates a cost of $34,850 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	410	$85	$34,850

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, review costs would total $1,400 ($70 x 20 supplements; $140 x 1 submission to the Docket). Based on an hourly wage rate of $40, project management costs would total $1,680 ($80 x 21 submissions).

15. Explanation for Program Changes or Adjustments

The requested burden hours for the 2010 ICR was 290 hours. ROCIS erroneously approved the total hours as 14 so the current total burden hours shows as 14 in ICRAS/ROCIS. Therefore, although ICRAS/ROCIS shows an increase in burden (from 14 to 410) the actual increase in burden is 290 to 410 (a difference of 120 hours) which results from an adjustment based on areview of the data we received on this ICR over the past few years.

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

There are no forms or other materials on which this information can be displayed.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.