Guidance for Industry
Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims
Supporting Statement

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.

In the Federal Register of March 13, 2008 (73 FR 13546), FDA published the draft guidance entitled "Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims." The draft guidance contained no information collection subject to OMB review under the PRA. The final guidance, however, contains two new provisions that are subject to OMB review and approval under the PRA, and one new provision that would be exempt from OMB review. Under the PRA, FDA must first obtain OMB approval for this information collection before we may issue the final guidance.

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. The intent of the guidance is to provide common labeling for antihypertensive drugs except where differences are clearly supported by clinical data.

3. Use of Improved Information Technology and Burden Reduction

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 would be no duplicate information collection under this guidance.

5. Impact on Small Businesses or Other Small Entities

The guidance would recommend 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 relating to the guidelines in 5 CFR 1320.5

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

On June 15, 2005, the Cardiovascular and Renal Drugs Advisory Committee met in open public session to discuss class labeling for cardiovascular outcome claims for drugs that are indicated to treat hypertension. The advisory committee voiced a broad consensus in favor of labeling changes to describe briefly the clinical benefits related to cardiovascular outcome expected from lowering blood pressure with any antihypertensive drug. The labeling proposed in this guidance is consistent with the advisory committee's recommendations.

A draft guidance of the same title was announced in the FEDERAL REGISTER on March 13, 2008, and comments were requested. Comments were received from industry, professional societies, and consumer groups on the draft guidance and were taken into consideration by FDA in finalizing this guidance.

In the Federal Register of March 22, 2010, FDA published an opportunity for public comment on the information collection that could result from the final guidance. 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 Act.

11. Justification for Sensitive Questions

There are no sensitive questions.

12. Estimates of Annualized Hour Burden and Costs

Burden-

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.

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 70 cardiovascular outcome claim supplements will be submitted annually from approximately 30 different companies, and that each supplement will take approximately 4 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.

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

Estimated Annual Reporting Burden

	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	30	2.33	70	4	280
TOTAL					290

Costs-

FDA estimates a cost of $23,200 for industry to submit the information collection requested in this guidance (290 hours x $80 per hour loaded wage rate).

13. Estimates of Other Total Annual Cost Burden to Respondents and Recordkeepers

There are no other industry costs, including capital costs or operating and maintenance costs, that would result from this guidance.

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 $5040 ($70 x 70 supplements; $140 x 1 submission to the Docket). Based on an hourly wage rate of $40, project management costs would total $5680 ($80 x 71 submissions).

15. Explanation for Program Changes or Adjustments

There are no program changes or adjustments.

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.

PAPERWORK REDUCTION ACT SUBMISSION

Please read the instructions before completing this form. For additional forms or assistance in completing this form, contact your agency's Paperwork Clearance Officer. Send two copies of this form, the collection instrument to be reviewed, the supporting statement, and any additional documentation to: Office of Information and Regulatory Affairs, Office of Management and Budget, Docket Library, Room 10102, 725 17th Street NW, Washington, DC 20503.

1. Agency/Subagency originating request

FDA

2. OMB control number b. [ ] None

a. 0910 -

3. Type of information collection (*check one*)

a. [x] New Collection

b. [ ] Revision of a currently approved collection

c. [ ] Extension of a currently approved collection

d. [ ] Reinstatement, without change, of a previously approved collection for which approval has expired

e. [ ] Reinstatement, with change, of a previously approved collection for which approval has expired

f. [ ] Existing collection in use without an OMB control number

For b-f, note Item A2 of Supporting Statement instructions

4. Type of review requested (*check one*)
a. [x] Regular submission
b. [ ] Emergency - Approval requested by at close of comment period
c. [ ] Delegated

5. Small entities
Will this information collection have a significant economic impact on a substantial number of small entities? [ ] Yes [x] No

6. Requested expiration date
a. [X] Three years from approval date b. [ ] Other Specify:____/___

7. Title Guidance on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims

8. Agency form number(s) (*if applicable*)

9. Keywords human drugs NDAs supplements

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

11. Affected public (*Mark primary with "P" and all others that apply with "x")*
a. ___ Individuals or households d. ___ Farms
b. _x_ Business or other for-profit e. ___ Federal Government
c. ___ Not-for-profit institutions f. ___ State, Local or Tribal Government

12. Obligation to respond (*check one*)
a. [x] Voluntary- (guidance document)
b. [ ] Required to obtain or retain benefits
c. [Mandatory

13. Annual recordkeeping and reporting burden
a. Number of respondents - 31_____
b. Total annual responses – 71_____
1. Percentage of these responses collected electronically – 25%
c. Total annual hours requested – 290 _____
d. Current OMB inventory – new collection___
e. Difference 0 _____

_____

14. Annual reporting and recordkeeping cost burden *(in thousands of dollars)*
a. Total annualized capital/startup costs 0_____
b. Total annual costs (O&M) 0_____
c. Total annualized cost requested 0_____
d. Current OMB inventory 0_____
e. Difference _____
f. Explanation of difference This is a proposed rule___
1. Program change _____
2. Adjustment _____

15. Purpose of information collection (*Mark primary with "P" and all others that apply with "X"*)
a. _ Application for benefits e._ Program planning or management
b. _ Program evaluation f._ Research
c. _ General purpose statistics g._x_ Regulatory or compliance
d. _ Audit

16. Frequency of recordkeeping or reporting *(check all that apply)*
a. [ ] Recordkeeping b. [ ] Third party disclosure
c. [x] Reporting
1. [x] On occasion 2. [ ] Weekly 3. [ ] Monthly
4. [ ] Quarterly 5. [ ] Semi-annually 6. [] Annually
7. [ ] Biennially 8. [ ] Other (describe) _

17. Statistical methods
Does this information collection employ statistical methods

18. Agency Contact (person who can best answer questions regarding the content of this submission)

[ ] Yes [x] No	Name: Elizabeth Berbakos Phone: _____

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