FOOD AND DRUG ADMINISTRATION

Additional Criteria and Procedures for Classifying Over-the-Counter Drugs as Generally Recognized as Safe and Effective and Not Misbranded; Guidance for Industry – *Time and Extent Applications for Nonprescription Drug Products*

OMB Control No. 0910-0688

SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA or we) regulations regarding "Time and Extent Applications for Nonprescription Drug Products." FDA's legal authority to regulate the ingredients contained in over-the-counter (OTC) drug products derives from sections 321, 351, 352, 353, 355, 360, and 371 of the Federal Food, Drug, and Cosmetics Act (the FD&C Act). FDA follows the procedures outlined in 21 CFR 330.10 for classifying active ingredients in OTC drug products as generally recognized as safe and effective (GRASE) and not misbranded.

Effective December 23, 2016, additional criteria and procedures by which OTC drugs initially marketed in the United States after the OTC drug review began in 1972, and OTC drugs without any U.S. marketing experience, may become eligible for consideration in the OTC drug monograph system (see 67 FR 3060). The regulations in 21 CFR 330.14 define a two-step process to include an ingredient in an OTC drug monograph (i.e., to classify the ingredient as GRASE for a particular purpose). First, to determine whether a drug product is eligible to be considered for inclusion in the OTC drug monograph system, certain information must be submitted to FDA in a "time and extent application" (TEA) to show that a drug product meets the criteria described in 21 CFR 330.14(b) (see 21 CFR 330.14(c) and (d)). Second, if the drug product is found eligible, FDA will publish a notice of eligibility in the Federal Register requesting that interested persons submit data to demonstrate the safety and effectiveness of the drug product for its OTC use(s) (21 CFR 330.14(f)). To assist respondents with the information collection provisions found in the regulations, FDA has created guidance regarding this process.

FDA, therefore, requests OMB approval of the information collection provisions found in 21 CFR 330.14 and the associated guidance entitled, *Guidance for Industry: Time and Extent Applications for Nonprescription Drug Products.*

2. Purpose and Use of the Information Collection

Respondents (private sector businesses) collect information under the provisions of 21 CFR 330.14 to substantiate that an ingredient or ingredients are eligible to be considered for inclusion in the OTC drug monograph system and, if so, to demonstrate that the ingredient or ingredients can be classified as GRASE. FDA uses the information collected to determine eligibility (first

part of two-step process) and, if determined eligible, to classify the ingredient(s) as GRASE or not GRASE (second part of the process).

3. Use of Improved Information Technology and Burden Reduction

FDA expects information to be collected, reviewed, compiled, and submitted electronically where possible. Based on our experience to date, FDA estimates that 95 percent or more of the responses will be submitted electronically. FDA no longer requires that collected information be submitted in hard copy and would prefer that the information be submitted electronically. Submissions received in the last several years have been exclusively (100 percent) in electronic format.

4. Efforts to Identify Duplication and Use of Similar Information

The data and information collected under the provisions of 21 CFR 330.14 do not duplicate any other data and information that may be available to FDA. No other FDA regulations require submission of the information required by 21 CFR 330.14(c) and (d). FDA may have data required by 21 CFR 330.14(f) and (i) if it was submitted under new drug applications (NDAs). In such situations, the data from NDAs can be cross-referenced to support the requirements of 21 CFR 330.14(f) and (i) and need not be resubmitted.

5. Impact on Small Businesses or Other Small Entities

There are no exceptions for small businesses/marketing enterprises. FDA provides assistance to small businesses through guidance on its website and through small business liaison component offices within the agency.

6. Consequences of Collecting the Information Less Frequently

The collections of information required under the provisions of 21 CFR 330.14 are one-time burdens for the submitting parties. This information is needed to determine whether the requirements of 21 USC 321(p) are satisfied.

7. Special Circumstances Relating to the Guidelines of 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 May 30, 2017 (82 FR 24716), but received no comments.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

Certain information submitted in a TEA or a safety and effectiveness submission may be considered confidential. Under 21 CFR 330.14(d), all TEAs are handled as confidential upon receipt until such time as a decision is made on the eligibility of the drug product. If the drug is found to be eligible for inclusion in the OTC drug monograph system, any information that FDA deems confidential under 18 U.S.C. 1905, 5 U.S.C. 552(b), or section 301(j) of the act will be removed from the TEA, and the remainder of the application will be placed on public display in the Division of Dockets Management when the notice of eligibility is published (21 CFR 330.14(d))). If the condition is not found to be eligible, the TEA will not be placed on public display, but a letter from FDA to the applicant stating why the condition was not found to be eligible will be placed on public display in the Division of Dockets Management (21 CFR 330.14 (d)).

Under 21 CFR 330.14(f), safety and effectiveness data submitted in response to a notice of eligibility will be made publicly available for viewing at the Division of Dockets Management, except data deemed confidential under 18 U.S.C. 1905, 5 U.S.C. 552(b), or section 301(j) of the act. Submissions must clearly identify data considered confidential under these provisions (21 CFR 330.14(f)). Proposed compendial standards will not be considered confidential (21 CFR 330.14(f)).

11. Justification for Sensitive Questions

There are no sensitive questions associated with the information collection.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Burden Estimate

FDA Estimates the burden of the information collection as follows:

Table 1 – Estimated Annual Reporting Burden[1]

21 CFR Part 330; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
330.14(c) and (d); Time and extent application and submission of information	2	1	2	1,525	3,050
330.14(f) and (i); Safety and effectiveness data	2	1	2	2,350	4,700
330.14(j)(3); sponsor request for informal conference	1	1	1	1	1
330.14(j)(4); sponsor signed statement that	2	1	2	1	2

21 CFR Part 330; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
submission is complete					
330.14(k)(l); sponsor request for FDA withdraw of TEA consideration	1	1	1	1	1
330.14(k)(2); sponsor request for FDA to not deem submission withdrawn	1	1	1	2	2
TOTAL					7,756

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

By final rule of November 23, 2016 (81 FR 84465), FDA revised the TEA regulations to establish timelines and performance metrics for review of non-sunscreen TEAs, and safety and effectiveness data submissions, as required by the *Sunscreen Innovation Act*:

- Section 330.14(j) clarifies the requirements on content and format criteria for a safety and effectiveness data submission, and provides procedures for FDA's review of the submissions and determination of whether a submission is sufficiently complete to permit a substantive review. Section 330.14(j)(3) describes the process for cases in which FDA refuses to file the safety and effectiveness data submission. Under §330.14(j)(3), if FDA refuses to file the submission, the agency will notify the sponsor in writing, state the reason(s) for the refusal, and provide the sponsor with 30 days in which to submit a written request for an informal conference with the agency about whether the agency should file the submission.

- Under §330.14(j)(4)(iii), the safety and effectiveness data submission must contain a signed statement that the submission represents a complete safety and effectiveness data submission and that the submission includes all the safety and effectiveness data and information available to the sponsor at the time of the submission, whether positive or negative. Under § 330.14(k)(1), FDA, in response to a written request from a sponsor, may withdraw consideration of a TEA submitted under § 330.14(c) or a safety and effectiveness data submission submitted under § 330.14(f).

- Under § 330.14(k)(2), a sponsor may request that FDA not withdraw consideration of a TEA or safety and effectiveness data submission.

12b. Annualized Cost Estimate

The preparation of two TEAs per year will cost approximately $171,300 annually (using a 2017 wage rate of $56.17 multiplied by the total number of burden hours associated with submissions [3,050 hours]). Similarly we calculated that preparation of safety and effectiveness data in support of TEA ingredients will cost approximately $264,000 per year ($56.17 per hour

times 4,700 hours). Thus, we estimate a total annualized cost of $435,300 per year ($171,300 plus $264,000).

13. Estimates of Other Total Annual Cost Burden 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 related to the collection of information have been absorbed through existing resource allocations.

15. Explanation for Program Changes or Adjustments

The information collection reflects an additional 6 hours of burden and 5 annual responses. By final rule of November 23, 2016 (81 FR 84465), FDA revised the TEA regulations to establish timelines and performance metrics for review of non-sunscreen TEAs, and safety and effectiveness data submissions, as required by the *Sunscreen Innovation Act*. We itemized these regulations and the corresponding burden estimate in both our 60-day and 30-day notices, and in Q12. of this supporting statement. We have consolidated, however, the individual provisions as they appear to the reader at www.reginfo.gov.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans for tabulation and publication and project time scheduled.

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

The OMB expiration date will be displayed as required.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.