Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed

OMB Control Number 0910-0513
SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(b)(1)) requires all new drug application (NDA) applicants to file, as part of the NDA, "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture[,] use, or sale of the drug." Section 505(c)(2) of the FD&C Act (21 U.S.C. 355(c)(2)) imposes a similar patent submission obligation on holders of approved NDAs when the NDA holder could not have submitted the patent information with its application. Under section 505(b)(1) of the FD&C Act, we publish patent information after approval of an NDA in the list entitled "*Approved Drug Products with Therapeutic Equivalence Evaluations*" (the Orange Book). If patent information is submitted after NDA approval, section 505(c)(2) of the FD&C Act directs us to publish the information upon its submission.

FDA regulations at §§ 314.50(h) (21 CFR 314.50(h)) and 314.53 (21 CFR 314.53) clarify the types of patent information that must and must not be submitted to FDA as part of an NDA, an amendment, or a supplement, and require persons submitting an NDA, an amendment, or a supplement, or submitting information on a patent after NDA approval, to make a detailed patent declaration using Form FDA 3542a and Form FDA 3542.

The reporting burden for submitting an NDA, an amendment, or a supplement in accordance with § 314.50 (a) through (f), and (k) has been estimated by FDA and the collection of information has been approved by OMB under OMB control number 0910-0001. We are not re-estimating these approved burdens in this document. Only the reporting burdens associated with patent submission and listing, as explained below, are estimated in this document.

The information collection requirements are as follows:

Section 314.50(h) requires that an NDA, an amendment, or a supplement contain patent information described under § 314.53.

Section 314.53 requires that an applicant submitting an NDA, an amendment, or a supplement, except as provided in § 314.53(d)(2), submit on Forms 3542 and 3542a, the required patent information described in this section.

Compliance with the information collection burdens under §§ 314.50(h) and 314.53 consists of submitting with an NDA, an amendment, or a supplement (collectively referred to as "application") the required patent declaration(s) on Form 3542a for each "patent that claims the drug or a method of using the drug that is the subject of the new drug application or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product" (§ 314.53(b)). Such patents claim the drug substance (active ingredient), drug product (formulation and composition), or method of use. If a patent is issued after the application is filed with FDA but before the application is approved, the applicant must submit the required patent information on Form 3542a as an amendment to the application, within 30 days of the date of issuance of the patent.

Within 30 days after the date of approval of an application, the applicant must submit Form 3542 for each patent that claims the drug substance (active ingredient), drug product (formulation and composition), or approved method of use for listing in the Orange Book. In addition, for patents issued after the date of approval of an application, Form 3542 must be submitted within 30 days of the date of issuance of the patent.

2. Purpose and Use of the Information Collection

We collect this information as part of the NDA or, in the case of subsequently issued patents, as amendments to the unapproved NDA. When the NDA is approved, we collect this information in a separate submission that lists the patents that claim the drug substance or drug product described in the approved NDA or supplement or that claim an approved method of using the drug. We use the patent information provided in Form 3542 to list patents in the list of approved drug products titled, "*Approved Drug Products with Therapeutic Equivalence Evaluations*" (the Orange Book). Federal law specifically requires us to publish such patent information. ANDA and 505(b)(2) applicants that rely upon FDA's finding of safety and/or effectiveness for a listed drug are required to submit an appropriate patent certification or statement for each patent listed in the Orange Book.

3. Use of Improved Information Technology and Burden Reduction

The regulations do not specifically require the use of automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of any duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

We estimate no impact on small entities. The regulations apply to small and large businesses

alike. FDA provides small business and industry assistance to respondents through the Center for Drug Evaluation and Research (CDER) and through the Division of Manufacturers Assistance and Training component in the Center for Biologics Evaluation and Research (CBER).

6. Consequences of Collecting the Information Less Frequently

Information collection schedule is consistent with statutory requirements.

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 February 2, 2016 (81 FR 5465). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

No payments or gifts are provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under these reporting requirements is protected under 21 CFR 314.430 and under 21 CFR part 20.

11. Justification for Sensitive Questions

The information collection does not contain questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimate –

The numbers of patents submitted to FDA for listing in the Orange Book in 2012, 2013, and 2014 were 458, 509, and 617 respectively, for an annual average of 528 (458 patents + 509 patents + 617 patents) / 3 years = 528 patents / year). Because many of these individual patents are included in multiple NDA submissions, there could be multiple declarations for a single patent. From our previous review of submissions, we believe that approximately 14 percent of the patents submitted are included in multiple NDA submissions, and thus require multiple

patent declarations. Therefore, we estimate that 74 (528 patents x 14 percent) patents will be multiple listings, and there will be a total of 602 patents (528 patents + 74 patents = 602 patents) declared on Form FDA 3542. We approved 86, 94, and 107 NDAs in 2012, 2013, and 2014 respectively, of which we estimate approximately 71% submitted patent information for listing in the Orange Book. The remaining NDAs submitted Form 3542 as required and declared that there were no relevant patents.

We also approved approximately 101, 101, and 110 NDA supplements in 2012, 2013, and 2014 respectively, for which submission of a patent declaration would be required. We estimate there will be 200 instances (based on an average of 96 NDA approvals and 104 supplement approvals per year) where an NDA holder would be affected by the patent declaration requirements, and that each of these NDA holders would, on average, submit 3.4 declarations (602 patent declarations + 74 no relevant patent declarations) /200 instances = 3.4 declarations per instance) on Form FDA 3542.

We filed 112, 116, and 113 NDAs in 2012, 2013, and 2014, respectively, and 112, 112, and 156 NDA supplements in 2012, 2013, and 2014 respectively, for which submission of a patent declaration would be required. We estimate there will be 241 instances (based on an average of 114 NDAs filed and 127 NDA supplements filed per year) where an NDA holder would be affected by the patent declaration requirements. We estimate, based on a proportional increase from the number of declarations for approved NDAs, that there will be an annual total of 819 declarations (241 instances x 3.4 declarations per instance = 819 declarations) on Form FDA 3542a submitted with these applications.

Based upon information provided by regulated entities and other information, we previously estimated that the information collection burden associated with § 314.50(h) (citing § 314.53) and FDA Forms 3542 and 3542a will be approximately 5 hours and 20 hours per response, respectively.

FDA requests OMB approval for the following information collection:

Table 1. – Estimated Annual Reporting Burden[1]

21 CFR Section § 314.50 (citing § 314.53)	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
Form FDA 3542a	241	3.4	819	20	16,380
Form FDA 3542	200	3.4	680	5	3,400
TOTAL					19,780

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

12b. Annualized Cost Burden Estimates –

Based on the hours estimated above, the burden hour costs for the reporting requirements would be as follows:

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
NDA applicants	19,780	$86	$1,701,080

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

There are no capital costs or operating and maintenance costs (or start-up costs or service costs) projected due to the minimal nature of the reporting requirements.

14. Annualized Cost to the Federal Government

CDER project managers devote approximately 15 minutes to the review of each application submitted to the agency to record that the patent form has been included. CDER's document room staff devote approximately 2 hours per day loading application-related data into our computers. CDER "Orange Book staff" devote approximately 2 hours per day transmitting the data from the forms into our database and then generating reports and other related tasks. CDER's Internet team devotes approximately 2 hours per month to the Internet publication of the data. Costs associated with the collection are captured under OMB Control No. 0910-0001.

15. Explanation for Program Changes or Adjustments

The information collection reflects an increase in burden of **424** additional responses and **5,960** hours, corresponding to an increase in the number of incoming NDAs, amendments and supplements detailing patent declarations using Forms FDA 3542a and 3542, as well as projections on the number of forms received and those we expect to receive. As a result we have adjusted our estimate accordingly.

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected under this requirement will not be published.

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.