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

Terms of Clearance: None.

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 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 reporting 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.

In a final rule titled "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" (68 FR 36676, June 18, 2003) (the June 2003 final rule) FDA clarified the types of patent information that must and must not be submitted to FDA as part of an NDA, an amendment, or a supplement. The June 2003 final rule also required 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 required forms (Form FDA 3542a and Form FDA 3542). Certain sections of the June 2003 final rule regarding the application of 30-month stays on approval of certain abbreviated new drug applications (ANDAs) and certain new drug applications submitted through the pathway described at section 505(b)(2) of the act (505(b)(2) applications), were superseded by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, enacted on December 8, 2003. The affected sections of the regulations issued in the June 2003 final rule — §§ 314.52(a)(3) and 314.95(a)(3) (21 CFR 314.52(a)(3) and 21 CFR 314.95(a)(3)) — were revoked by the technical amendment to the June 2003 final rule published in the Federal Register of March 10, 2004 (69 FR 11309).

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

The information that is collected is not already available to FDA for the specific drug product at issue in the NDA, or an amendment or supplement to the NDA. Only the NDA applicant or the NDA holder may submit patent information regarding the drug to FDA. FDA's patent listing function is ministerial, and FDA relies upon the patent information submitted by the NDA applicant or NDA holder to fulfill the statutory requirement to publish such information.

FDA is the only agency that reviews and approves NDAs, 505(b)(2) applications, and ANDAs. We thus have not undertaken literature searches or contacted staff of other organizations with respect to this information collection. Section 505(b)(1) of the FD&C Act requires NDA applicants to file patent information as part of the NDA. Sections 505(b) and 505(j) of the FD&C Act require 505(b)(2) and ANDA applicants to provide an appropriate patent certification or

statement for each patent listed in the Orange Book for the listed drug(s) relied upon or reference listed drug, respectively. A 505(b)(2) or ANDA applicant that submits a patent certification under section 505(b)(2)(A)(iv) or 505(j)(2)(A)(vii)(A) of the FD&C Act, respectively, certifying that the patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted (paragraph IV certification), is required to send notice of the paragraph IV certification to each patent owner and the NDA holder as part of the application process. Therefore, no duplication of data exists.

The importance of obtaining such data relates to adherence to the law and regulatory requirements for submission of patent information, and ensuring that ANDA and 505(b)(2) applicants adhere to the legal and regulatory requirements for providing an appropriate patent certification or statement for each patent listed in the Orange Book for the listed drug(s) relied upon or reference listed drug, respectively. Adherence to those requirements, in turn, governs whether and when we can approve such ANDAs and 505(b)(2) applications.

5. Impact on Small Businesses or Other Small Entities

As discussed in the "Analysis of Economic Effects" section of the June 2003 final rule, this information collection does not have a significant impact on a substantial number of small entities.

6. Consequences of Collecting the Information Less Frequently

Failure to collect the information could result in incomplete, erroneous, or misleading patent information being listed by FDA and prompt 505(b)(2) and ANDA applicants to provide incomplete patent certifications, thereby exposing those applicants to potential litigation for patent infringement. Ultimately, the failure to collect the information could have an adverse effect on the protection of patented drug products and on the availability of generic drug products.

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

The reporting requirements are consistent with the guidelines in 5 CFR 1320.5(d)(2). To the extent that the regulations require reporting to occur more frequently than the quarterly basis described in §1320.5(d)(2)(i) in certain circumstances (e.g., submission of patent information within 30 days of issuance of a new patent), this is expressly required by section 505(c)(2) of the FD&C Act. The regulations do not require submission of duplicate copies of reports.

We do not require respondents to keep records more than 3 years. No statistical data is used. The collection does not include a pledge of confidentiality. Respondents are not required to submit trade secrets, proprietary, or other confidential 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 June 17, 2013 (78 FR 36193). FDA received one comment from a private citizen. The comment stated, generally, that "it would be appropriate to require, along with the submission of any patents on the original drug and its formulation, any associated patents or claimed patent submission on metabolites or secondary products of the original drugs."

(FDA Response) FDA disagrees with the comment. FDA's regulations at § 314.53(b) (21 CFR 314.53(b)) prohibit submission of drug substance (active ingredient) patents claiming metabolites when the metabolite is not the active ingredient described in the NDA. Section 314.53(b) states, in relevant part: "For patents that claim the drug substance, the applicant shall submit information only on those patents that claim the drug substance that is the subject of the pending or approved application or that claim a drug substance that is the same as the active ingredient that is the subject of the approved or pending application. * * * Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section, and information on these patents must not be submitted to FDA." FDA clarified the criteria for listing

patent information in the Orange Book in response to a request by the Federal Trade Commission (FTC) in its July 2002 report on "Generic Drug Entry Prior to Patent Expiration: An FTC Study" (see 68 FR 36676; June 18, 2003, and http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf). FDA determined that a patent claiming a metabolite does not claim an approved drug and thus does not meet the statutory requirements for listing in the Orange Book (see 67 FR 65448 at 65451; October 24, 2002). However, if a patent claims an approved method of using an approved drug to administer a metabolite, the submission of the patent would be permissible as long as all of the conditions for submitting ''method-of-use'' patents are met (see 68 FR 36676 at 36680; June 18, 2003). Section 314.53(c)(2)(i)(M)(4) and 314.53(c)(2)(ii)(N)(4) require that an applicant submit on Forms 3542a or 3542, as appropriate, information on whether a drug substance patent claims only a metabolite of the active ingredient that is described in the application or supplement, so that FDA can determine whether the patent is eligible for listing in the Orange Book (see section 2.5 of Forms 3542a and 3542).

9. Explanation of Any Payment or Gift to Respondents

FDA did not provide any payment or gifts 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

No questions of a sensitive nature are asked.

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 2010, 2011, and

2012 were 351, 329, and 458 respectively, for an annual average of 379 (351patents + 329 patents + 458 patents) / 3 years = 379 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 53 (379 patents x 14 percent) patents will be multiple listings, and there will be a total of 432 patents (379 patents + 53 patents = 432 patents) declared on Form FDA 3542. We approved 84, 93, and 86 NDAs in 2010, 2011, and 2012 respectively, of which 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, 83, and 101 NDA supplements in 2010, 2011, and 2012 respectively, for which submission of a patent declaration would be required. We estimate there will be 183 instances (based on an average of 88 NDA approvals and 95 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 2.8 declarations (432 patent declarations + 76 no relevant patent declarations) / 183 instances = 2.8 declarations per instance) on Form FDA 3542. We filed 96, 91, and 112 NDAs in 2010, 2011, and 2012 respectively, and 100, 91, and 112 NDA supplements in 2010, 2011, and 2012 respectively, for which submission of a patent declaration would be required. We estimate there will be 201 instances (based on an average of 100 NDAs filed and 101 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 563 declarations (201instances x 2.8 declarations per instance = 563 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 3542a and 3542 will be approximately 20 hours and 5 hours per response, respectively.

FDA requests OMB approval for the following information collection:

Table 1. – Estimated Annual Reporting Burden

21 CFR Section § 314.50 (citing § 314.53)	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Form FDA 3542	183	2.8	512	5	2,560
Form FDA 3542a	201	2.8	563	20	11,260
Total					13,820

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	13,820	$85	$1,174,700

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

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

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.

15. Explanation for Program Changes or Adjustments

Our estimated burden hours for this information collection has decreased from 14,120 hours to 13,820 hours. As described in #12 above, this decrease is the result of new data and projections on the number of forms we have received and will receive.

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

We do not seek an exemption from displaying the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.