

OMB INFORMATION COLLECTION

Docket No. 02n-0417

Supporting Statement

Applications for FDA Approval to Market a New Drug: Patent 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 (0910-0513)

A. Justification

1. Circumstances Necessitating Information Collection

The Food and Drug Administration (FDA) is proposing to amend its regulations regarding the content and format of new drug applications (NDAs), 505(b)(2) applications (the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355)) (Tab A), and abbreviated new drug applications (ANDAs). The final rule (Tab B) would clarify the types of patents that NDA applicants must submit to FDA and revise the patent declaration statement (forms FDA 3542 and 3542a) (Tab C) submitted by NDA applicants. The proposal would also revise the regulations regarding the effective date of approval for certain ANDAs and 505(b)(2) applications. Under federal law, if an ANDA or 505(b)(2) application contains a certification stating that the patent covering the reference listed drug is invalid or will not be infringed, the applicant must provide a notice of certification of invalidity or noninfringement to the NDA holder and to the patent owner. If a lawsuit for patent infringement is brought within 45 days of the notice, federal law prevents FDA from making the approval of an ANDA or 505(b)(2) application effective for 30 months (although this period may be shortened or lengthened by court decision or court order). The proposal would state that the 30-month stay in the effective date of an ANDA or 505(b)(2) application operates only once, and this would have the effect of reducing the number of notices that ANDA and 505(b)(2) application applicants must provide to NDA applicants and to patent owners.

FDA requests Office of Management and Budget (OMB) approval of the information collection requirement in "Applications for FDA Approval to Market a New Drug: Patent 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," 21 CFR 314.50, 314.52, 314.53, 314.94 and 314.95 (Tab D). The agency estimates that the proposed rule's total information collection is 499,805 hours. This information is needed to ensure compliance with the statutory and regulatory requirements that information concerning patents that claim a drug, or a method of using a drug, that is the subject of a pending or approved NDA be submitted to us if they could reasonably form the basis of a patent infringement lawsuit. The form is designed to ensure that all such patents are submitted, and that only information concerning patents that satisfy the statutory and regulatory requirements is submitted.

Section 505(b)(1) requires NDA applicants to file with the application the patent number and

the expiration date of any patent which claims the drug for which the applicant submitted the application 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. If a patent which claims such drug is issued after the filing date but before approval of the application, the NDA applicant must file this same information with respect to the new patent. Under Section 505(c)(2), if a patent is issued after approval of the NDA, the holder must file this same information within 30 days after the date that the patent involved is issued.

21 CFR 314.50(h) and 314.53(b) and (c) - Reporting

This provision would be affected by the changes described in proposed §§ 314.53(b) and (c). In brief, § 314.50(h) instructs NDA applicants to submit the patent information described in § 314.53. Proposed § 314.53(b) would clarify the types of patents that NDA applicants must submit, while proposed § 314.53(c) would revise the two patent declarations that NDA applicants must submit. The revised patent declarations would require NDA applicants to provide greater detail regarding the claims that cover the drug product that is the subject of an NDA, amendment to an NDA, or an NDA supplement.

21 CFR 314.52(a)(3), 314.94(a)(12) and 314.95(a)(3) - Reporting

These provisions would pertain to 505(b)(2) application applicants and to ANDA applicants respectively. In brief, the proposal would have the effect of requiring these applicants to send only one notice of invalidity of noninfringement of patent to NDA holders and to patent owners if the applicant certifies that the patent is invalid or will not be infringed.

2. How, by Whom, and for What Purpose Information Used

We will collect this information as part of the NDA or, in the case of later-obtained patents, as amendments to the NDA. When the NDA is approved, we will collect this information in a separate submission that reflects the patents that cover the drug as we have approved it, including the specific methods of use of the drug for which we granted approval.

We use the patent information in the reports to list patents in our approved drug products list titled, "Approved Drug Products With Therapeutic Equivalence Evaluations." Federal law specifically requires us to publish such patent information. ANDA and 505(b)(2) application applicants can then consult the listed patent information to prepare their patent certification statements or to identify patents that claim a specific drug substance, drug product, or method of use for that product.

3. Consideration of Information Technology

The rule would not specifically prescribe the use of automated, electronic, mechanical, or other technological collection techniques or other forms of information technology. Respondents are free to use whatever forms of information technology that may best assist them in complying with the rule.

4. Efforts to Identify Duplication and Similar Information Already Available

The information that is collected is not already available to FDA. Such information is available only from NDA applicants and NDA holders, and will vary for each drug. Because our patent listing function is ministerial, only the NDA applicant or NDA holder has the ability to identify the patents for which relevant information is to be submitted.

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 act requires NDA applicants to provide patent information as part of the NDA. Sections 505(b) and 505(j) of the act require certain 505(b)(2) application applicants and ANDA applicants to provide a notice of certification of invalidity or noninfringement of patent to patent owners and NDA holders in certain situations; this notification is 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 patent submissions, and ensuring that ANDA and 505(b)(2) applicants adhere to the appropriate legal and regulatory requirements for certifying to those patents. Adherence to those requirements, in turn, governs whether and when we can approve such ANDA and 505(b)(2) applications.

5. Small Business

This information collection would not have a significant impact on small businesses.

6. Consequences of Less Frequent Information Collection and Technical or Legal Obstacles

Failure to collect the information could result in incomplete, erroneous, or misleading patent information being listed by FDA and prompt 505(b)(2) application applicants and ANDA applicants to make incorrect 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. Consistency with the Guidelines in 5 CFR 1320.5(d)(2)

The final rule's reporting requirements are consistent with the guidelines in 5 CFR 1320.5(d)(2). The final rule would not require reporting to occur more frequently than the quarterly basis described in §320.5(d)(2)(i), nor would it require multiple copies of the reports.

We will 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. Consultation Outside the Agency

The agency relied on its expertise with these applications to estimate the amount of time and cost needed to prepare the reports described in the rule. As required by section 3506(c)(2)(B) of the Paperwork Reduction Act of 1995 (PRA), FDA provided opportunity for public comment on the information collection requirements of the proposed rule that published in the Federal Register on October 24, 2002 (Vol. 67, No. 206, p. 65448) (Tab E). The proposed rule received over 35 comments to which FDA responded in the preamble of the final rule.

9. Payment or Gift to Respondents

FDA did not provide any payment or gifts to respondents.

10. Confidentiality of Information

Assurances of confidentiality (beyond those already existing in federal law and FDA regulations) are unnecessary.

11. Sensitive Questions

No questions of a sensitive nature are asked.

12. Estimates of Burden Hours and Explanation

In 1998-2002, the annual number of original applications we have received containing a certification of invalidity or noninfringement of patent (paragraph IV certification) has been 61, 58, 79, 90, and 82, respectively. The annual average is 74 $((61 \text{ certifications} + 58 \text{ certifications} + 79 \text{ certifications} + 90 \text{ certifications} + 82 \text{ certifications}) / 5 \text{ years} = 74 \text{ certifications/year})$. Because the final rule requires notice of a paragraph IV certification filed in the original ANDA or 505(b)(2) application or when the application is amended to include a paragraph IV certification or when such notice did not provide a full opportunity for a 30-month stay, this would mean that these applicants would usually provide only one notice to NDA holders and patent owners, and would provide a second notice only in the rare instance when the ANDA or 505(b)(2) applicant on its own initiative cut short the 45 day period following notice. We increase the frequency of response to account for these rare second notices. There may still be multiple certifications made by ANDA or 505(b)(2) applicants which will not require notice. In previous estimates, we have combined the information collection burden for both the notice and the certification. For purposes of the final rule, we assume that the certification information collection burden is 4 hours and the information collection burden for the notice is 12 hours. We also account for the multiple number of certifications that may have to be provided by an ANDA or 505(b)(2) applicant. Under pre-existing regulations, we have had NDA holders submit two or more patents for a single NDA. While this may continue to occur, we believe that the final rule may reduce the number of patents submitted for listing because we have clarified the type of patents that must be submitted. The number of patents submitted could increase because we allow polymorph patents to be submitted or it could decrease if no test data exist to demonstrate that a drug

product containing the polymorph will perform the same as the drug product contained in the NDA. We, thus, estimate the number of annual certifications at 1.5×74 (the number of original certifications). Thus, the information collection burden for §§ 314.50(i)(1)(i) and 341.94(a)(12) (certifications) would be 444 hours (74 respondents \times 1.5 response per respondent \times 4 hours per response = 444 hours). The information collection burden for §§ 314.52(a)(3) and 314.95(a)(3) (notices) would be 897 hours (74 respondents \times 1.01 response per respondent \times 12 hours per respondent).

To estimate the number of enhanced patent declarations that will be submitted annually, we referred to historical data on patent submissions. For the years 1998-2002, the numbers of patents submitted to us were 159, 205, 321, 280, and 268 respectively, for an annual average of 246.6 ((159 patents + 205 patents + 321 patents + 280 patents + 268 patents) / 5 years = 247 patents per year). Because many of these individual patents are included in multiple NDA submissions, there could be multiple declarations for a single patent. From our review of submissions, we believe the duplicate patent listings to be 20 percent of the number of unique patents. Therefore, we estimate 49.2 (246.6 patents \times 20 percent) patent declarations will be multiple listings, and there will be 296 (247 declarations + 49 declarations = 296 declarations) total annual patent declarations. As we received 115 and 99 NDAs in 2000 and 2001, respectively, we assume there will be 107 ((115 applications + 99 applications) / 2 years = 107 applications/year) instances where an NDA holder would be affected by the patent declaration requirements and that each of these holders would, on average, submit 2.8 (296 declarations / 107 instances = 2.8) declarations per instance.

However, § 314.53(b) and (c) have different impacts on the hours per response. On the one hand, § 314.53(b) might decrease the reporting burden because it would specify certain patents that must not be submitted, and thus discourage NDA applicants and holders and patent owners from submitting information on those patents. On the other hand, § 314.53(b) will require NDA applicants and holders or patent owners to submit patent information on different forms of the active ingredient described in the NDA, and this could result in more patent information being submitted or less patent information if test data do not exist to demonstrate that a drug product containing the polymorph will perform the same as the drug product described in the NDA. We cannot determine whether the potential net effect will increase, decrease, or not change the overall burden associated with submitting patent information, so we have not assigned any change in the total reporting burden for the change in patent information alone.

In contrast, 314.53(c) makes the patent declaration more detailed. The change in the declaration will increase the burden hours per response under § 314.50(h) (the provision under which we covered patent declarations described in § 314.53(c)) because respondents will be required to be more precise in their declarations. Based on other rules that require respondents to compile and submit information in their possession, we estimate that the two new patent declaration will result in an additional information collection burden of 18 hours. However, the previous burden hour estimate of 1,666 hours for § 314.50 covered paragraphs (a) through (f), in addition to paragraphs (h) and (k). We are unable to determine how many of the 1,666 hours were devoted to patent declarations, so we simply add 18 hours to the 1,666 hour estimate for § 314.50(a) through (f), (h), and (k), resulting in a burden hour

estimate of 1,684 hours (1,666 hours + 18 hours) to account for a respondent's need for more time to make and verify the patent declaration. Thus, the information collection burden for § 314.50(a) through (f), (h), and (k) will increase to 498,464 hours (296 annual responses x 1,684 hours per response = 498,464 hours).

The overall reporting burden is as follows:

Table 1.-Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	Frequency of Responses	Total Annual Responses	Hours per Response	Total Hours
314.50(a) - (f), (h), (k) (citing 21 CFR 314.53) Forms FDA 3542 and 4542(a)	107	2.8	296	1,684	498,464
314.50(i)(1)(i) and 314.94(a)(12)	74	1.5	111	4	444
314.52(a)(3) and 314.95(a)(3)	74	1.01	74	12	897
Total					499,805

Burden Costs

We estimate the annual reporting cost associated with this rule to be \$293,999 (not including previous cost estimates for § 314.50(a) through (f) and (k), which the final rule does not amend). Based on the total average hourly compensation of \$55.14, the cost would be \$992 (\$55.14 per hour x 18 hours per declaration) per event.¹ The burden on individual firms would depend on the number of declarations they submit, but the estimated annual burden to all declarants would be \$293,000 (\$992 per declaration x 295.8 events).

13. Annual Cost to Respondents

There are no total capital or start-up costs or service costs projected for this rule due to the minimal nature of the recordkeeping and reporting requirements.

14. Annual Cost to the Government

We estimate the annualized cost to the federal government to be negligible. While we cannot

¹ Hourly rate for "lawyer" from 2000 National Compensation Survey (<http://www.bls.gov/ncs/ocs/sp/ncbl0402.pdf>) is \$38.70, adjusting for inflation at 2.85% (unadjusted CPI-U) and 40% benefits.

predict whether the final rule would result in an increase, decrease, or no change in the volume of patent information submitted to FDA, our patent duties are solely ministerial and consist largely of listing patent information in "Approved Drug Products With Therapeutic Equivalence Evaluations."

The proposed change regarding the 30-month stay and its potential to reduce the number of notices going from ANDA and 505(b)(2) applicants to NDA holders and patent owners would have little or no direct impact on the federal government because we do not receive copies of these notices. We do receive documentation to show that the NDA holder and patent holder received notice from the ANDA or 505(b)(2) applicant, but this is a ministerial action and, other than filing the documentation as part of the ANDA or 505(b)(2) application, we take no action regarding such documentation. Furthermore, because we estimate that the number of notices would decrease by 37 (from 37 respondents filing two notices per year to 37 respondents filing only one notice per year), we believe the government's cost savings associated with 37 pieces of documentation are also negligible.

15. Changes from Previous Approval

The rule would represent a slight increase over the previous information collection burden.

16. Statistical Reporting

Information collected under this requirement will not be published.

17. Exemption for Display of Expiration Date

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

18. Exemption to Certification Statement

We are not requesting any exemption from the certification statement identified in Item 19 of form OMB Form 83-1.