U.S. Food & Drug Administration
Applications for FDA Approval to Market a New Drug
OMB Control No. 0910 0001

SUPPORTING STATEMENT **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA) regulations. Specifically, under section 505(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA or the act) (21 U.S.C. 355(a)), a new drug may not be commercially marketed in the United States, imported, or exported from the United States, unless an approval of an application filed with FDA under section 505(b) or 505(j) of the act is effective with respect to such drug. Under the act, it is the sponsor's responsibility to provide the information needed by FDA to make a scientific and technical determination as to whether the product is safe and effective for use. Regulations regarding the approval of new drug applications are codified under 21 CFR Part 314, and include information collection provisions. To assist respondents in this regard, FDA has created the following:

- Form FDA 0356h[1] (and instructions): *Application to Market a New or Abbreviated New Drug or Biologic for Human Us*e;
- Form FDA 2252 (and instructions): *Transmittal of Annual Reports for Drugs and Biologics For Human Use* (21 CFR 314.81);
- Form FDA 2253 (and instructions): *Transmittal of Advertisements and Promotional Labeling For Drugs and Biologics For Human Use*; and
- Forms FDA 3331/3331a: *Field Alert Report* and Instruction

Therefore, unless otherwise noted, this information collection requests approval for the provisions found in the associated regulations, accompanying forms, and discussed in this supporting statement.

2. Purpose and Use of the Information Collection

Section 505 of the FFDCA requires that a new drug may not be marketed unless the manufacturer provides FDA with scientific evidence that the drug is both safe and effective. The regulations at 21 CFR part 314 state: *[t]he purpose of this part is to establish an efficient and thorough drug review process in order to: (a) Facilitate the approval of drugs shown to be safe and effective; and (b) ensure the disapproval of drugs not shown to be safe and effective. These regulations are also intended to establish an effective system for FDA's surveillance of marketed drugs.* Therefore, without the information provided by respondents regarding the drug products they seek to market, we would not be able to adequately protect the public health by assuring

[1] Burden associated with Form FDA 0356h is approved under OMB Control No. 0910-0338: *General Licensing Provisions: Biologics License Application, Changes to an Approved Application, Labeling, Revocation and Suspension (21 CFR Part 601).*

their safety and efficacy.

3. Use of Improved Information Technology and Burden Reduction

We encourage the electronic submission of information required under part 314, and have issued several guidance documents describing the process for submitting information in electronic format. These guidance documents and others 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

We are unaware of duplicative information collection. In some cases, regulations may warrant the establishment of an independent information collection request. For example, some, but not all, applications may be associated with patent information; and some, but not all, applications may require labeling for specific populations. In such cases and where relevant in this supporting statement, we have cross -referenced the applicable OMB Control No.

5. Impact on Small Businesses or Other Small Entities

The regulations at 21 CFR Part 314 do not provide exemptions for small businesses. However, FDA has established various agency components to assist small businesses in complying with our regulations. Contact information may be found on our website at https://www.fda.gov. Additionally, and as mentioned above, FDA's Center for Drug Evaluation and Research (CDER) has issued guidance on a variety of topics associated with new and abbreviated drug applications. These documents are developed to assist respondents with the regulatory requirements and are available online.

6. Consequences of Collecting the Information Less Frequently

Information collection schedule is consistent with statutory requirements under the FFDCA.

7. Special Circumstances Relating to the Guidelines in 5 CFR 1320.5(d)(2)

There are the following special circumstances relating to the information collection: (1) sections of 21 CFR 314 require reporting in less than 30 days – these are postmarketing reports and expedited notification to FDA and are necessary to determine as soon as possible whether a threat to the public health exists that warrants immediate regulatory action; (2) more than an original and 2 copies of a submission is required (e.g., four copies of draft labeling or 12 copies of final printed labeling) in order to permit concurrent (and, consequently, quicker) review of the application; (3) although applicants are required to submit proprietary, trade secret, and other confidential information, this information is protected under FDA regulations and the FFDCA (see number 10 below); and (4) the specific format and content requirements for application submissions is necessary to ensure complete submissions (and reduce the need for time-consuming resubmissions) and to assist FDA in efficient reviews.

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

In the Federal Register of May , 26, 2017 (82 FR 24351) FDA published a notice soliciting public comment on the information collection. One comment was received suggesting that human drug and biologic applicants be required to include a preliminary Structured Benefit Risk (SBR) table upon submission of applications for marketing approval. As discussed in our 30-day notice of December 12, 2017, (82 FR 58403), while we appreciate and are considering this suggestion, because the regulations currently impose no such requirement, we have made no adjustments to the information collection. In addition to seeking public input through notice and comment in the Federal Register, we regularly obtain informal feedback through our participation in conferences and workshops sponsored by trade organizations such as *The Food and Drug Law Institute*, *The Drug Information Association*, *The Pharmaceutical Research and Manufacturers of America*, and *The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use*.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is 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. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 310(j) of the FFDCA.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Table 1 – Estimated Annual Reporting Burden

21 CFR Part 314	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
SUBPART B – APPLICATIONS					
314.50(a)-(g)[2], (i)-(l)--Content and format of a 505(b)(1) or 505(b)(2) application	378	1.33	503	1,921	966,263

[2] 21 CFR 314.50(h) requires patent information and burden is approved under OMB Control No. 0910-

21 CFR Part 314	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
314.52--Non-infringement of patents (NDAs)	7	3	21	16	336
314.95--Non-infringement of patents (ANDAs)	209	3	627	16	10,032
314.60--Amendments	564	9.96	5,618	80	449,440
314.65--Withdrawal of unapproved applications	27	71.63	1,934	2	3,868
314.70 and 314.71--Supplements and submissions	838	7.04	5,897	150	884,550
314.72--Change of ownership	142	2.04	289	2	578
314.80-Postmarketing reporting of adverse drug experiences[3]	-	-	-	-	-
314.81--Other postmarketing reports and 314.81(b)(1) field alert reports	342	19.98	6,834	8	54,672
314.81(b)(2)--Annual reports	913	5.07	4,632	40	185,280
314.81(b)(3)(i) --Promotional labeling	529	81.66	43,198	2	86,396
314.81(b)(3)(iii)-withdrawal from sale[4]	-	-	-	-	-
SUBPART C – ABBREVIATED APPLICATIONS					
314.93-Petition to request a change from a listed drug[5]	-	-	-	-	-
314.94(a) and (d)--ANDA content	180.5	3.75	676.5	480	324,720
314.96(a)(1)--Amendments to unapproved ANDAs	514	26.66	13,647	80	1,091,760

0513: *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*.

[3] Burden approved under OMB Control Nos. 0910-0230 (*Postmarketing Adverse Drug Experience Reporting*) and 0910-0291 (*FDA's MEDWATCH Program – Paper Reporting*).

[4] Burden approved under OMB Control No. 0910-0045: *Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution*.

[5] Burden approved under OMB Control No. 0910-0191: *Administrative Practices and Procedures; Formal Evidentiary Public Hearing*.

21 CFR Part 314	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
314.97--Supplements to ANDAs	343	17.57	6027	80	482,160
314.98-Postmarketing reports[6]					
314.99(a)--Responsibilities of ANDA Applicants	265	7.04	1867	2	3,734
SUBPART D – FDA ACTION ON APPLICATIONS AND ABBREVIATED APPLICATIONS					
314.101(a)—ANDA filing	1	1	1	.5 (30 min.)	.5
314.103-Dispute resolution	75	2	150	5	750
SUBPART G – MISCELLANEOUS PROVISIONS					
314.420--Drug Master Files	500	2.06	1,028	61	62,708
SUBPART H – ACCELERATED APPROVAL OF NEW DRUGS FOR SERIOUS OR LIFE-THREATENING ILLNESSES					
314.550--Promotional material and subpart H applications	29	7.76	225	120	27,000
TOTAL					4,634,247.5

The estimates above are based on our experience with the information collection. Other relevant regulations are discussed as follows:

Section 314.95 requires that any notice of certification of invalidity or non-infringement of a patent to each patent owner and the NDA holder be sent by ANDA applicants. Burden hours for § 314.95 are approved under OMB Control No. 0910-0786: *Abbreviated New Drug Applications and 505(b)(2) Applications*.

Section 314.96 sets forth requirements for amendments to an unapproved ANDA and section 314.97 sets forth requirements for submitting supplements to an approved ANDA for certain changes to the application (burden hours for § 314.96 and 314.97 are approved under OMB Control No. 0910-0786 are therefore not included in table 1 above);

Section 314.107 – *Abbreviated New Drug Applications and 505(b)(2) Applications* provisions, unless otherwise specified, are approved under OMB Control No. 0910-0786 – *id*.;

section 314.110(b)(3) states that, after receipt of an FDA complete response letter, an applicant must either 1) resubmit the application addressing all the deficiencies identified in the complete response letter, 2) withdraw the application, or 3) request an opportunity for a hearing on the question of whether there are grounds for denying approval of the application. The burden hours for § 314.110(b)(3) are included under parts 10 through 16 (21 CFR parts 10 through 16)

[6] Burden approved under OMB Control Nos. 0910-0230 (*Postmarketing Adverse Drug Experience Reporting*) and 0910-0291 (*FDA's MEDWATCH Program – Paper Reporting*).

hearing regulations, in accordance with § 314.201 and are OMB approved in 0910-0191.

Section 314.122(a) requires that an ANDA or a suitability petition that relies on a listed drug that has been voluntarily withdrawn from sale must be accompanied by a petition seeking a determination whether the drug was withdrawn for safety or effectiveness reasons. The burden hours for § 314.122(a) are approved under OMB Control No. 0910-0191.

Section 314.122(d) sets forth requirements for relisting petitions for unlisted discontinued products. The burden hours for § 314.122(d) are approved under OMB Control No. 0910-0191.

Sections 314.125 and 314.127 state that FDA may refuse to approve an NDA or an ANDA and will provide the applicant written notice of an opportunity for a hearing under section 314.200 along with the reason for refusal to approve the application, including lack of a patent certification or statement with respect to each listed patent for an approved drug product that is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted and was approved before the original 505(b)(2) was submitted. The burden hours for section 314.125 and 314.127 (refuse to approve an ANDA) are approved by OMB and are included under parts 10 through 16 (21 CFR parts 10 and 16) hearing regulations, in accordance with § 314.201. The burden hours for these collections are approved under OMB Control No. 0910-0191.

Section 314.126(c) sets forth requirements for a petition to waive criteria for adequate and well-controlled studies. The burden hours for § 314.126(c) are approved by OMB under 0910-0191 Sections 314.150(a) and (b) and 314.151(a) and (b) set forth requirements for the withdrawal of approval of an NDA or ANDA and the applicant's opportunity for a hearing and submission of comments. The burden hours for § 314.151(a) and (b) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201. This information collection burden is approved by OMB in 0910-0191.

Section 314.151(c) sets forth the requirements for withdrawal of approval of an ANDA and the applicant's opportunity to submit written objections and participate in a limited oral hearing. (The burden hours for § 314.151(c) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, approved by OMB under OMB control number 0910-0191.

Section 314.153(b) sets forth the requirements for suspension of an ANDA when the listed drug is voluntarily withdrawn for safety and effectiveness reasons, and the applicant has an opportunity to present comments and participate in a limited oral hearing. The burden hours for § 314.152(b) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved under OMB Control No. 0910-0191.

Section 314.161(b) and (e) sets forth the requirements for submitting a petition to determine whether a listed drug was voluntarily withdrawn from sale for safety or effectiveness reasons. The burden hours for § 314.161(b) and (e) are approved under OMB Control No. 0910-0191.

Section 314.200(c), (d), and (e) requires that applicants or others subject to a notice of

opportunity for a hearing who wish to participate in a hearing file a written notice of participation and request for a hearing as well as the studies, data, and so forth, relied on. Other interested persons may also submit comments on the notice. This section also sets forth the content and format requirements for the applicants' submission in response to notice of opportunity for hearing. (The burden hours for § 314.200(c), (d), and (e) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved under OMB Control No. 0910-0191.

Section 314.200(f) states that participants in a hearing may make a motion to the presiding officer for the inclusion of certain issues in the hearing. The burden hours for § 314.200(f) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved under OMB Control No. 0910-0191.

Section 314.200(g) states that a person who responds to a proposed order from FDA denying a request for a hearing provide sufficient data, information, and analysis to demonstrate that there is a genuine and substantial issue of fact which justifies a hearing. The burden hours for § 314.200(g) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved under OMB Control No. 0910-0191.

Section 314.420 states that an applicant may submit to FDA a drug master file in support of an application, in accordance with certain content and format requirements.

Section 314.430 states that data and information in an application are disclosable under certain conditions, unless the applicant shows that extraordinary circumstances exist. (The burden hours for § 314.430 are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved in OMB 0910-0191.

Section 314.530(c) and (e) states that if FDA withdraws approval of a drug approved under the accelerated approval procedures, the applicant has the opportunity to request a hearing and submit data and information. The burden hours for § 314.530(c) and (e) are included under parts 10 through 16 hearing regulations, in accordance with § 314.201, and are approved in OMB 0910-0191.

Section 314.530(f) requires that an applicant first submit a petition for stay of action before requesting an order from a court for a stay of action pending review. (The burden hours for § 314.530(f) are already approved in OMB 0910-0194.

Section 314.550 requires an applicant with a new drug product being considered for accelerated approval to submit copies of all promotional materials to the FDA during the preapproval and post-approval periods.

Section 314.610(b)(1) requires that applicants include a plan or approach to postmarketing study commitments in applications for approval of new drugs when human efficacy studies are not ethical or feasible, and provide status reports of postmarketing study commitments. (The information collection burden estimate for § 314.610(b)(1) is included in table 1 under the

estimates for §§ 314.50 (a), (b), (c), (d), (e), (f), (k) and (l) and 314.81(b)(2)).

Section 314.610(b)(3) requires that applicants propose labeling to be provided to patient recipients in applications for approval of new drugs when human efficacy studies are not ethical or feasible. (The information collection burden estimate for § 314.610(b)(3) is included in table 1 under the estimates for § 314.50(e)).

Section 314.630 requires that applicants provide postmarketing safety reporting for applications for approval of new drugs when human efficacy studies are not ethical or feasible. The burden hours for § 314.630 are already approved by OMB under OMB 0910-0230 and 0910-0291.

Section 314.640 requires that applicants provide promotional materials for applications for approval of new drugs when human efficacy studies are not ethical or feasible. (The information collection burden estimate for § 314.640 is included in table 1 above under the estimates for § 314.81(b)(3)(i)).

12b. Annualized Cost Burden Estimate

FDA estimates an average pharmaceutical industry wage rate of $75.00 per hour for preparing and submitting the information collection requirements under 21 CFR 314. When multiplied by the burden hours above, the cost to respondents is estimated at $347,512,312.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

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

14. Annualized Cost to the Federal Government

FDA has allocated 835 FTEs to reviewing submissions under 21 CFR 314. Where the cost of each FTE is approximately $175,000 (fully-loaded), the total cost burden to the Federal Government is estimated at $146,125,000.

15. Explanation for Program Changes or Adjustments

The estimated burden for the information collection reflects an increase of **1,212,941** annual hours and **7,429** annual responses. We have made this adjustment based on updated data on the number of drug applications we have received. Also, we have revised the IC list appearing at www.reginfo.gov by consolidating the 17 previously itemized regulatory provisions into 4 elements. We believe this will assist the reader by more easily identifying the summary of cumulative fluctuations for the collection. At the same time, readers may still view estimated burden associated with individual provisions by referring to our 60-day and 30-day notices and in the burden table found at Q.12: *Estimates of Annualized Burden Hours and Costs* of this supporting statement.

16. Plans for Tabulation and Publication and Project Time Schedule

FDA does not intend to publish tabulated results of these information collection requirements.

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

Display of the OMB Expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.