UNITED STATES FOOD & DRUG ADMINISTRATION

Applications for FDA Approval to Market a New Drug
21 U.S.C. 355; 21 CFR Part 314

OMB Control No. 0910-0001 – Revision

SUPPORTING STATEMENT **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

STATUTORY AUTHORITY AND RELEVANT REGULATIONS

This information collection supports implementation of section 505 of the Federal Food, Drug, and Cosmetic Act (FFDCA); Food and Drug Administration (FDA, the agency, us or we) regulations; agency and industry program performance goals established in accordance with user fee authority; and associated guidance. Section 505 of the FFDCA (21 U.S.C. 355) governs procedures and requirements for the submission and review of applications and abbreviated applications to market a new drug, including amendments, supplements, and postmarketing reports to and for those applications. We have promulgated regulations in 21 CFR part 314 setting forth content and format requirements for new drug applications (NDAs) and abbreviated new drug applications (ANDAs), that include associated recordkeeping and disclosure requirements. Both the FFDCA and our implementing regulations explain a sponsor's responsibility to provide us with information needed to make a scientific and technical determination as to whether a product is safe and effective for use. For more information regarding new drug applications generally visit our website at: www.fda.gov/drugs/types-applications/new-drug-application-nda. We are revising the information collection to consolidate related activity from approved collections, finding this better utilizes our limited resources and provides a more cohesive view of agency operations. We are also revising the collection to include additional legal authorities and updated forms.

Section 505 and implementing regulations

In accordance with section 505 of the FFDCA, "*[n]o person shall introduce into interstate commerce any new drug, unless and approval an application filed pursuant to this [provision] is effective with respect to such drug*." As stated previously, our regulations in 21 CFR part 314 establish NDA and ANDA submission requirements and associated information collection. The estimate of the average industry burden we provide to account for information collection activity associated with satisfying the requirements in section 505 of the FFDCA and 21 CFR part 314 is cumulative, although in determining our estimate we list specific provisions in our burden table at Question 12 of this supporting statement to show the basis for our calculations. These provisions identify tasks such as reporting, documenting, recording, and disclosing information.

Unless otherwise discussed, the scope of this information collection, therefore, is intended to cover all requirements found in section 505 of the FFDCA and regulations in 21

CFR part 314. Where the applicability of a regulation in this part triggers information collection found in other agency statutes or regulations, we have included relevant discussion of and reference to associated, approved information collections. For example, 21 CFR 314.50(c)(2)(i) provides that, "*[t]he proposed text of the labeling, including, if applicable, any Medication Guide required under part 208 of this chapter, for the drug, with annotations to the information in the summary and technical sections of the NDA that support the inclusion of each statement in the labeling, and, if the NDA is for a prescription drug, statements describing the reasons for omitting a section or subsection of the labeling format in §201.57 of this chapter*." Upon referring to 21 CFR § 201.57 (specific requirements on content and format of labeling for human prescription drug and biological products) we note the the approved information collection request under OMB control no. 0910-0572 has been established to account for burden associated with these requirements. Similarly, burden associated with patient medication guides required under 21 CFR § 208 is accounted for under OMB control no. 0910-0393. We also try to explain the functional and operational relationship among the statutory and regulatory requirements pertaining to the governance of new drugs and drugs approved for human use as set forth in the FFDCA.

"User Fee" Legislation and Agency Commitment Goals

Provisions in the FFDCA, as amended by the Prescription Drug User Fee Act (PDUFA) and Generic Drug User Fee Act (GDUFA), authorize us to asses fees in conjunction with the submission of NDAs and ANDAs. User fees facilitate agency review of applications and engage stakeholders in establishing review priorities and dedicating limited agency resources. The FDA Reauthorization Act of 2017 (FDARA) (Pub. Law 115-52) sets forth our current commitment goals, incorporating specific requirements that augment provisions found in the FFDCA and agency regulations and direct the development of agency guidance. These provisions are set forth in the document entitled, " *PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022*," (hereafter *Commitment Goals*) which is posted to our website at: https://www.fda.gov/media/99140/download, and attached to this supporting statement. FDARA also added section 506I to the FFDCA which imposes additional reporting requirements on NDA and ANDA holders regarding the marketing status of approved drug products.

Our Office of Financial Management (OFM) is responsible for managing the financial aspects of our user fee programs and maintains an accounts receivable system used for invoicing, collections, reporting, and data maintenance. We have established and maintain the following information collections in support of the corresponding user fee programs:

- Prescription Drug User Fee Program – OMB control no. 0910-0297;
- Generic Drug User Fee Program – OMB control no. 0910-0727; and
- Biosimilars User Fee Program – OMB control no. 0910-0718.

In administering the programs we utilize "*cover sheets*" for invoicing and agency tracking purposes, and have developed agency guidance to provide respondents with instructions on

topics such as payment of fees, waivers, reductions, refunds, and reconsiderations. In this request, we account for information collection burden attendant to marketing submissions and activities necessary for the efficient and thorough review of drug safety and effectiveness, as well as appropriate systems of surveillance for marketed drugs. The information collection determined necessary for each application shall be construed in light of these objectives. The various user fee acts require the HHS Secretary to submit annual performance reports to Congress for each fiscal year during which fees are collected. These annual performance reports document our success in meeting these goals and are made publicly available on our website.

EFFORTS AT OUTREACH AND AVAILABILITY OF RESOURCE MATERIAL

Forms

We have developed the following forms, noting statutory and regulatory requirements mandate the electronic submission of applications unless a waiver has been granted.

- Form FDA 0356h (and instructions): *Application to Market a New or Abbreviated New Drug or Biologic for Human Use*;
- 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
- Forms FDA 3542 and 3542a
- New Form FDA 3938: *Drug Master File* (21 CFR 314.420).

Individuals requesting printed forms are instructed to contact the FDA Forms Manager by email at formsmanager@OC.FDA.GOV. Certain fees may be applicable.

Guidance Documents

Consistent with regulations in 21 CFR parts 314.50 (content and format of NDAs), 314.94 (content and format of ANDAs), and 314.445 (guidance documents), we maintain and make publicly available guidance documents that apply to 21 CFR part 314. The guidance documents are issued in accordance with our Good Guidance Practice regulations in 21 CFR part 10.115, which provide for public comment at any time, invite respondent participation in their development, and inform respondents to the collection that a person is not required to respond to a collection of information unless it displays a valid control number. Guidance documents issued consistent with these regulations are intended to help respondents comply with the requirements of section 505 of the FFDCA and implementing regulations in 21 CFR 314. FDA maintains a searchable guidance database at www.fda.gov/regulatory-information/search-fda-guidance-documents. We also issue topic-specific guidance documents as identified in our Performance Goals Commitment Letter, and consistent with our GGP regulations, that provide for public comment and respondent

participation in their development. Finally, our Center for Drug Evaluation and Research publishes an annual guidance agenda announcing both draft and final guidance documents in development.

Templates

We have created templates to support information collection associated with drug master files covered in part 314.420 at Drug Master File (DMF) Templates | FDA. Drug master files (DMFs) are submissions to FDA used to provide confidential, detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of human drug products allowing respondents to reference material without disclosing DMF contents to those parties. DMFs are not required by statute or regulation, nor are they approved nor disapproved. Rather, FDA reviews the technical contents of DMFs in connection with the review of applications that reference them (e.g., NDAs, ANDAs, INDs, BLAs). The purpose of the DMF is to clearly identify DMF *Holder* and *Agent* information, and to facilitate submission and archive of DMF correspondence in electronic format. The information collected includes the organization, DMF holder, DMF agent, contact information, type of DMF, submission type (original or amendment), establishment information, and certifications.

We are therefore requesting OMB approval of the information collection provisions associated with applications for FDA approval to market a new drug as set forth in section 505 of the FFDCA (21 U.S.C. 355) and agency regulations; associated forms and guidance issued under parts 21 CFR 10.115, 314.50, 314.445, and the most recent reauthorization performance goals included in FDARA, each as 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. We intend to use the information as set form in 21 CFR part 314: *[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 their safety and efficacy.

We also use product approval and related patent and exclusivity information to publish the "*Approved Drug Products with Therapeutic Equivalence Evaluations"* list (the Orange Book). More information regarding the Orange book is available from our website at www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book.

3. Use of Improved Information Technology and Burden Reduction

We encourage the electronic submission of information as 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 specific information collections not included here with the applicable OMB control no. in which we account for any attendant burden.

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

The information collection schedule is consistent with statutory requirements set forth in the FFDCA, applicable agency regulations, and FDA and Industry user fee performance goals.

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 November 16, 2020 (85 FR 73057) we published a notice inviting public comment on the proposed collection of information. No comments were received.

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; Information Collection (IC) Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
SUBPART B – APPLICATIONS					
314.50; content and format of a 505(b)(1) or 505(b)(2) application	378	1.33	503	1,921	966,263
314.52 and 314.53; non-infringement of patents (NDAs) and submission of patent information	7	3	21	16	336
314.55; pediatric use information	-	-	0	-	0
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[2]	-	-	0	-	0
314.81; other postmarketing reports: (b)(1); field alert reports	342	19.98	6,834	8	54,672
***(b)(2); annual reports	913	5.07	4,632	40	185,280
***(b)(3)(i); promotional labeling	529	81.66	43,198	2	86,396

21 CFR Part 314; Information Collection (IC) Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
314.90; waivers					
SUBPART C – ABBREVIATED APPLICATIONS					
314.93; petition to request a change from a listed drug[1]	-	-	0	-	0
314.94; ANDA content	180.5	3.75	676.5	480	324,720
314.95; non-infringement of patents (ANDAs)	209	3	627	16	10,032
314.96; amendments to unapproved ANDAs	514	26.66	13,647	80	1,091,760
314.97; supplements to ANDAs	343	17.57	6027	80	482,160
314.98; postmarketing reports	-	-	0	-	0
314.99; responsibilities of ANDA Applicants	265	7.04	1867	2	3,734
SUBPART D – FDA ACTION ON APPLICATIONS AND ABBREVIATED APPLICATIONS					
314.101; filing an NDA and receiving an ANDA	1	1	1	.5 (30 min.)	.5
314.102; communications between FDA and applicants	1,620	3.8	6,153	13.55	83,386
314.103; dispute resolution	18	1	18	8	144
314.107; notice and copies of court notification	247	2	494	.5 (30 min.)	247
SUBPART E – HEARING PROCEDURES FOR NEW DRUGS					
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					
314.540; postmarketing safety reporting[2]	-	-	0	-	0
314.550; promotional material and subpart H applications[1]	-	-	0	-	0
TOTAL					4,202,264

We have included burden attendant to this activity in our estimate of burden associated with 314.50.

[2] Postmarket drug reporting is covered in collections 0910-0230, 0910-0291, and 0910-0645.

The estimates above are based on our experience with the information collection and reflect what we believe is the cumulative industry average burden associated with the information collection. Regulations in subpart A (§§ 314.1 through 314.3) set forth general provisions, while regulations in subparts B and C (§§314.50 through 314.99) set forth content and format requirements for new drug applications (NDAs) and abbreviated new drug applications (ANDAs) respectively. The regulations include requirements for the submission of specific data elements along with patent information, pediatric use information, supplements and amendments, proposed labeling, and specific postmarketing reporting provisions, and withdrawal of applications. Reporting provisions in part 314.80 are accounted for in

1 We have included burden attendant to this activity in our estimate of burden associated with 314.50.

collections approved under OMB control. no. 0910-0230, established for post-marketing drug adverse event reporting; and control nos. 0910-0291 and 0910-0645, established in support of our paper-based and electronic MedWatch reporting programs, respectively.

Part 314.102 provides for communications between FDA and NDA and ANDA sponsors. We are consolidating burden currently approved under OMB control no. 0910-0429 into this collection. Facilitating communication between FDA and product sponsors is included among the PDUFA performance goals. Agency regulations at 21 CFR §§ 312.47(b)(1)(ii), (b)(1)(iv), and (b)(2) describe information that should be submitted in support of a request for an End-of-Phase 2 meeting and a Pre-New Drug Application (NDA) meeting[2], and regulations in 21 CFR 314.102 describe other meetings and how to request them. We have developed guidance that assists sponsors of drug and biological drug products to align with PDUFA performance goals. The guidance document entitled, "*Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*," (discusses the principles of good meeting management and describes procedures for requesting, scheduling, conducting, and documenting formal meetings with FDA. Specifically, the guidance document identifies different meeting types that may be requested by sponsors of PDUFA product applications (including biological drug products) covered by agency regulations and includes content, format, and procedural information intended to facilitate discussion.

We are also consolidating burden associated with dispute resolution currently approved under OMB control no. 0910-0430. Ensuring adequate dispute resolution procedures to provide for appropriate review of scientific controversies between the FDA and members of regulated industry is also included among the user fee performance goals and established in section 562 of the FFDCA. Applicable regulations are found in part 314.103. The guidance document "*Formal Dispute Resolution: Sponsor Appeals Above the Division Level*," (November 2017) discusses agency procedures intended to address scientific and/or medical disputes between a sponsor and CDER or CBER as such disputes relate to the sponsor's application for a product covered by user fee goals. The guidance also identifies agency contact information and describes information that we recommend be included when seeking resolution to the scientific disputes discussed.

Regulations in subpart D governing FDA action on applications may require follow-up information collection directed to specific applicants, however we include petitions that may be submitted in accordance with Part 10 of our regulations in OMB control no. 0910-0191 (administrative practices), including hearing procedures discussed in 21 CFR part 314, subpart E. Miscellaneous provisions in subpart G include 314.420 pertaining to drug master files (DMFs). DMFs can be used to support, but are not substitutes for, applications reviewed by FDA. We have developed resources on our internet site https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs for respondents' use in support of new drug applications (NDAs), abbreviated new drug applications (ANDAs), and investigational new

2 Information collection provisions in 21 CFR 312 (Investigational New Drug (IND) regulations) are approved under OMB Control No. 0910-0014; information collection provisions in 21 CFR 314 (NDAs) are approved under OMB Control No. 0910-0001; and information collection provisions in 21 CFR 601 (BLAs) are approved under 0910-0338.

drug applications (INDs) under the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Finally, provisions in section 314.610 require 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 for status reports of postmarketing study commitments. The regulations also require that applicants propose labeling. We account for this burden in our reporting estimate under 314.50.

12b. Annualized Cost Burden Estimate

We assume 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 $315,184,800.

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. These costs are supplemented by industry submission of program user fees for prescription and generic drug application approvals.

15. Explanation for Program Changes or Adjustments

The information collection reflects changes and adjustments. Consolidating information collection associated with meeting requests, certain dispute resolutions, and drug master files results in an increase associated with provisions in subparts D and G. At the same time we have decreased our estimate associated with submissions under subpart B based on current data. The overall change to the collection is an increase in annual responses by **50,642**, with a decrease in hours by **-434,572**.

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.