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 those 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 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 assess and collect 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 User Fee Reauthorization Act of 2022 includes the reauthorization of PDUFA VII and GDUFA III, respectively, from fiscal years (FY) 2023 through 2027. The agency's commitment goals developed together with stakeholders outline implementation of individual activities. Additional information regarding user fee authorization is available from our website at https://www.fda.gov/industry/fda-user-fee-programs.

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;
- Biosimilars User Fee Program – OMB control no. 0910-0718;
- Electronic User Fee Refund Requests – OMB control no. 0910-0805.

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.

Covered Product Authorizations

Under the CREATES Act of 2019 (enacted as part of the Further Consolidated Appropriations Act of 2020 (21 U.S.C. 355-1(1) and 355-2)), developers of potential drug and biological products may use the CREATES pathway to obtain samples of brand products needed to support product applications, otherwise referred to as Covered Product Authorizations (CPAs). Instructions on obtaining a CPA is available from our website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/how-obtain-covered-product-authorization, respective to the following submission types:

- New drug applications submitted under section 505(b)(2) of the FFDCA;
- Abbreviated drug applications submitted under section 505(j) (information collection approved in control no. 0910-0727), and
- Biosimilar products submitted under section 351(k) of the Public Health Service Act (42 U.S.C. 262 et seq.) (information collection approved in control no. 0910-0718).

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 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 (and instructions): *NDA/ANDA Field Alert Report* and Instruction
- Revised Form FDA 3542 (and instructions): *Patent Information Submitted Upon and After Approval of an NDA or Supplement* (title change; editorial changes to selection

box instructions);

- Revised Form FDA 3542a (and instructions): *Patent Information Submitted with an NDA, Amendment, or Supplement* (revised to allow multiple selections of submission types (e.g., annual report and withdrawal of letter of authorization) and updates to the electronic logic to format the numbers requested in the form (e.g., Holder DUNS Number – limited to 9 digits, Establishment DUNS Number – limited to 9 digits, Registration (FEI) Number – limited to 10 digits);
- Revised Form FDA 3938 (and instructions): *Drug Master File* (21 CFR 314.420).
- Forms FDA 3988 and 3989 (and instructions): *Transmittal of Postmarketing Requirements (PMR)/Postmarketing Commitments (PMC)/Annual Status Report Information (PMR/PMC)*

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 Letters, 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 marketing applicants to reference material in their applications without disclosing the DMF contents to those marketing applicants. 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). Original DMFs, amendments, and DMF

correspondence must be submitted electronically in accordance with eCTD specifications. 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 (see FDA *"Guidance for Industry: Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications"* (February 2020)).

We are therefore requesting OMB approval of the information collections authorized by section 505 of the FFDCA (21 U.S.C. 355) and 21 CFR 314 for FDA approval to market a new drug, as implemented in the applicable forms, guidance, and commitment goals 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 for human use. We intend to use the information as set forth 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.* Without the information, FDA is unable to assure the safety and efficacy of drug products.

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 21 CFR 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. We reference relevant information collections approved in our current inventory as appropriate throughout this document.

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 applications by multiple reviews; (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 Q-10 below); and (4) the specific format and content requirements for application submissions are 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 September 28, 2023 (88 FR 66853), 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

The Privacy Act of 1974

In preparing this supporting statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected. This ICR collects personally identifiable information (PII). PII is collected in the context of the subject individuals' professional capacity and the FDA-related work performed for their employer (e.g., point of contact at a regulated entity). The PII is collected using the Electronic Submission Gateway and includes a

username and password. FDA determined that although PII is collected, the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, the contractor or FDA does not use name or any other personal identifier to retrieve records from the information collected. Through appropriate form and webpage design, FDA limited submission fields and minimized the PII collected to protect the privacy of the individuals.

The Freedom of Information Act (FOIA)

Under FOIA (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information. 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

The regulations include specific data elements. The 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 reports (PMRs). Respondents to the information collection are sponsors of these applications.

Regulations in subpart D (§§ 314.100 through 314.170) explain FDA actions on applications and set forth timeframes for FDA review. The information collection includes provisions established through our Agency user fee programs, most recently authorized under the FDA User Fee Reauthorization Act of 2022. These provisions pertain to performance goals, expedited programs, review transparency, communications with FDA, dispute resolution, drug safety enhancements, and the allocation of Agency resources to align with these program objectives as agreed to with our stakeholders and set forth in our "User Fee Performance Goals for Fiscal Years 2023-2027" Commitment Letters, which are available from our website at https://www.fda.gov along with more information about specific FDA user fee programs/

Included among the provisions in subpart G (§§ 314.410 through 314.445), § 314.420 covers information to include in drug master files (DMFs). To assist respondents to this information

collection we have prepared templates, guidance, forms, and resources available from our website at www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs. We have developed Form FDA 3938 and accompanying instructions on submitting DMFs in accordance with the applicable regulations. We are revising Form FDA 3898 and the accompanying instructions to allow for multiple selections of submission types and to clarify the number of digits to be entered for the holder and establishment registration numbers.

In accordance with § 314.445, we also develop Agency guidance documents to assist respondents in complying with provisions in part 314. These guidance documents are issued consistent with our good guidance practice regulations at 21 CFR 10.115. To search available FDA guidance documents, visit our website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Applications submitted in accordance with subpart H (§§ 314.500 through 314.560) pertain to accelerated approval of new drugs for serious or life-threatening illnesses.

Information collection and associated burden for the submissions in subpart I (§§ 314.600 through 314.650) pertain to approval of certain new drugs when human efficacy studies are not ethical or feasible. The regulations provide for the submission of specific data elements, animal studies of safety and efficacy to establish likely clinical benefit in humans and upon approval of the drug product, additional requirements and/or restrictions to ensure safe use of the product. Additional PMRs, safety reporting, and promotional material as well as requirements for withdrawal of these human drug applications, and FDA termination of requirements for these human drug applications are included in §§ 314.620 through 314.650. The estimated burden for these human drug applications is included in the reported submissions and burden under general human drug applications, § 314.50, and other specific regulations in the table for human drug application requirements in general.

Finally, included in our estimated burden is effort we attribute to information collection activities associated with CPAs, as discussed above in Q-1.

12a. Annualized Hour Burden Estimate

Table 1--Estimated Annual Reporting Burden[1]

21 CFR Part 314 – Information Collection (IC) Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Subpart B - Applications					
314.50(a)-(l)--Content and format of a 505(b)(1) or 505(b)(2) application	85	1.42	121	1,921	232,441
314.50(i)(1)--Patent certifications: Form FDA 3542	170	6.55	1,113	10	11,130
314.50(i)(1)--Patent certifications: Form FDA 3542a	1	1	1	15	15

314.50(i)(6) Amended patent certifications	73	4.33	316	2	632
314.52(a), (b), and (e) – NDAs--Notice of noninfringement of patent certification	15	3	45	15	675
314.52(c)--Noninfringement of patent certification notice content	22	3	66	0.33 (20 minutes)	22
314.53(f)(1)--Correction of patent information errors by persons other than the NDA holder	7	1.14	8	10	80
314.53(f)(2)--Correction of patent information errors by the NDA holder	8	1.13	9	1	9
314.60--Amendments to unapproved NDA, supplement or resubmission	269	7.22	1,942	80	155,360
314.60(f)--Patent certifications for unapproved applications	6	1	6	2	12
314.65--Withdrawal of unapproved applications	20	1.05	21	2	42
314.70 and 314.71--Supplements and other changes to approved application	501	5.13	2,570	150	385,500
314.72--Changes of ownership of NDAs	73	1.67	122	2	244
314.81--Other PMR 314.81(b)(1) [3331 and 3331a field alert reports and follow-ups]	532	18.5	9,834	8	78,672
314.81(b)(2) - [Form FDA 2252]--Annual reports	692	4.46	3,090	40	123,600
314.81(b)(2) - [Form FDA 2253]--Promotional labeling	310	121	37,508	2	75,016
314.81(b)(2)(vii) Form FDA 3988--PMR/PMC	737	0.87	642	24	15,408
314.81(b)(2)(vii) Form FDA 3989--PMR/PMC Annual Status Report for Drugs and Biologics	737	0.29	216	24	5,184
Subpart C – ABBREVIATED APPLICATIONS					
314.93 Suitability Petitions	16	1.31	21	24	504
314.94(a) and (d)--ANDA content	213	4.02	857	480	411,360
314.94(a)(12)(viii) Amended patent certifications before approval of ANDA	153	1	153	2	306
314.95(c)--Noninfringement of patents (ANDAs)	209	3	627	16	10,032
314.96(a)(1)--Amendments to unapproved ANDAs	514	26.55	13,647	80	1,091,760

314.96(c) Amendment for pharmaceutical equivalent to a listed drug other than reference listed drug	1	1	1	300	300
314.96(d)--Patent certification requirements	100	1	100	2	200
314.97--Supplements and other changes to ANDAs	343	17.57	6,027	80	482,160
314.97(b) Supplements to ANDA for pharmaceutical equivalent to a listed drug other than RLD	1	1	1	300	300
314.99(a)--ANDA Applicants: Withdrawal of unapproved ANDAs	58	2.41	140	2	280
314.99(a)--ANDA Transfer of ownership	137	1.24	170	2	340
Subpart D – FDA ACTINO ON APPLICATNIOS					
314.101(a)--NDA or ANDA filing over protest	1	1	1	0.5 (30 minutes)	0.5
314.107(e)--notification of court actions or written consent to approval	54	1.98	107	0.5 (30 minutes)	53.5
Subparts G, H, and I					
314.420--Drug Master Files – original Form FDA 3938	491	2.05	1,005	61	61,305
DMF Amendments – Technical	1,335	18.71	24,979	8	199,832
DMF Amendments - REMS	2	1	2	8	16
DM Amendments - administrative	1,024	9.67	6,851	6	41,106
DMFs--Annual reports	1,836	6.04	11,097	4	44,388
314.550--Promotional material and subpart H applications[2]	69	5.84	403	120	48,360
CPA Requests for NDA/Biologics License Application Products	1	1	1	5	5
Total					3,476,650

[1]Total burden hours have been rounded.
[2]We have included burden attendant to subpart H applications activity in our estimate of burden associated with § 314.50.

12b. Annualized Cost Burden Estimate

We assume an average pharmaceutical industry wage rate of $85.00 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 $295,514,825.

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 $325,348 (fully-loaded), the total cost burden to the Federal Government is estimated at $271,665,580. These costs are supplemented by industry submission of application and program user fees for prescription and generic drug applications and approved products.

15. Explanation for Program Changes or Adjustments

Our estimated burden for the information collection reflects an overall decrease of 725,814 hours and 22,149 responses annually. While this is consistent with our summary burden table that published in the *Federal Register* with our 60- and 30-day notices, we note an inadvertent error in the calculated decrease in our publications (-642,293.5). The reporting period for this information collection renewal includes the 3 years of the COVID-19 pandemic. We attribute this adjustment to a decrease in the number of submissions received during the public health emergency.

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.