4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-N-2440]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Biologics License Applications Procedures and Requirements

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments (including recommendations) on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to https://www.reginfo.gov/public/do/PRAMain. Find this particular information collection by selecting "Currently under Review---Open for Public Comments" or by using the search function. The OMB control number for this information collection is 0910-0338. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Biologics License Applications (BLAs) Procedures and Requirements

OMB Control Number 0910-0338--Extension

This information collection supports Agency regulations and recommendations found in associated guidance pertaining to BLA procedures and requirements. A BLA is a request for permission to introduce, or deliver for introduction, a biological product into interstate commerce (§ 601.2 (21 CFR 601.2)). BLAs are regulated under parts 600 through 680 (21 CFR parts 600 through 680). A BLA is submitted by any legal person or entity who is engaged in manufacture or an applicant for a license who takes responsibility for compliance with product and establishment standards. Interested persons may visit https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/biologics-license-applications-bla-process-cber for additional information, including available Agency resources.

Regulations in part 601 set forth applicable procedures for the submission of license application information, including content and format elements. The regulations also explain requirements for suspension, revocation, and reissuance of BLAs and communicate procedures for requesting a hearing. Additionally, the information collection includes the submission of manufacturing change information governed by section 506A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 356a), as well as postmarketing reports for approved human drugs and licensed biological products governed by section 506B of the FD&C Act (21 U.S.C. 356b). Finally, regulations in parts 610 through 680 establish both general and specific biological product standards.

To implement these provisions, we have developed the following collection instruments:

1. Forms

Form FDA 356h, *Application to Market a New or Abbreviated New Drug or Biologic for Human Use*, provides a uniform format for submitting BLAs. Form FDA 356h is a fillable PDF form that may be submitted through our Electronic Submission Gateway (ESG), for which respondents must create and maintain a user account. Utilizing Form FDA 356h helps to ensure

that an application is complete and contains all the necessary information, so that delays due to lack of information may be avoided. In addition, the form provides key information to FDA for efficient handling and distribution to the appropriate staff for review. We have recently made minor updates to Form FDA 356h resulting from the October 3, 2022, reauthorization of the Prescription Drug User Fee Act. In this collection we account for BLAs submitted using Form FDA 356h.

Form FDA 2252, *Transmittal of Annual Report for Drugs and Biologics for Human Use*, is used by an applicant of a licensed biological product to submit annual reports required by § 601.70(b) (21 CFR 601.70(b)). Form FDA 2252 is also a fillable PDF form and approved in OMB control number 0910-0001; however, in this information collection we account for submissions pertaining to biological products.

Form FDA 2253, *Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use*, was developed for use by respondents to transmit specimens of advertisements and promotional labeling (e.g., circulars, package labels, container labels, etc.), as well as labeling changes. The submission of this information is required by § 601.12 (21 CFR 601.12) for biological products and by 21 CFR 314.81 for drug products. Form FDA 2253 is a fillable PDF form and is approved for use in OMB control number 0910-0001; however, in this information collection we account for submissions pertaining to biological products.

Form FDA 3674, *Certificate of Compliance Under 42 U.S.C. 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank*, was developed for use by respondents to certify submissions as required by section 402(j)(5)(B) of the Public Health Service (PHS) Act and is submitted through our ESG. Form FDA 3674 is a fillable PDF form and is approved for use in OMB control number 0910-0616; however, in this information collection we account for submissions pertaining to biological products.

2. Cover Sheets

As provided for under § 601.2(a), we also utilize cover sheets, so denoted for purposes of identifying specific content information within a given application.

3. Guidance Documents

The guidance document "Cooperative Manufacturing Arrangements for Licensed Biologics," (November 2008), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cooperative-manufacturing-arrangements-licensed-biologics, discusses strategies for meeting an increased need for flexible manufacturing arrangements. Since cooperative manufacturing arrangements can take a considerable amount of time to develop, the guidance is intended to be useful for planning purposes in the early phases of product development. Many companies that perform only limited aspects of manufacturing processes are interested in sharing or contracting parts of manufacturing to facilitate product development and manufacturing flexibility. The guidance discusses recommended communication between licensed manufacturers and contract manufacturers regarding changes to production and facilities, results of tests and investigations regarding the product, types of products manufactured in the contract facility, and standard operating procedures. We believe that the information collection provisions in the guidance do not create a new burden for respondents. We believe the reporting and recordkeeping provisions are part of usual and customary business practices.

All Agency guidance documents issued are consistent with our good guidance practice regulations in 21 CFR 10.115, which provide for public comment at any time. We maintain a searchable database of our guidance documents at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Respondents to this collection of information are licensed manufacturers of biological products. Based on the number of 2021 fiscal year application submissions, we estimate there are 371 such respondents. The total annual responses are based on the number of submissions (i.e., license applications, labeling and other supplements, protocols, advertising and promotional

labeling, notifications) for a particular product received annually by FDA. The hours per response are based on informal communications with industry and our experience with the information collection.

In the *Federal Register* of November 1, 2022 (87 FR 65776) we published a 60-day notice soliciting comment on the proposed collection of information. No comments were received.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Section or Other Citation; Activity	Form FDA No.	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours[2]
601.2(a) and 610.60 through 610.65; Application for biologics license (includes labeling)	356h	51	1.078	55	860	47,300
601.5(a); Requirement to notify FDA of intention to discontinue manufacture of a product or all products	NA	17	1.0589	18	0.33 (20 minutes)	6
601.6(a); Requirement to provide FDA with copy of notification to selling agents and distributors upon suspension of its license	NA	1	1	1	0.33 (20 minutes)	1
601.12(a)(5); Requirement to inform FDA of changes to an approved application	NA	327	10.263	3,356	1	3,356
601.12(b)(1), (b)(3), and (e); Requirement to inform FDA of changes to an approved application	356h	195	5.795	1,130	80	90,400
601.12(c)(1) and (3); Requirement to inform FDA of changes to an approved application	356h	153	4.6536	712	50	35,600
601.12(c)(5); Requirement to inform FDA of changes to an approved application	356h	73	2.740	200	50	10,000
601.12(d)(1), (d)(3), and (f)(3); Requirement to inform FDA of changes to an approved application	356h	279	3.398	948	24	22,752
601.12(f)(1); Requirement to inform FDA of changes to an approved application	2253	64	2.75	176	40	7,040
601.12(f)(2); Requirement to inform FDA of changes to an approved application	2253	66	1.758	116	20	2,320

601.12(f)(4) and 601.45; Requirement to inform FDA of changes to an approved application	2253	173	340.416	58,892	10	588,920
601.27(b); Request for deferred submission of some or all safety and effectiveness assessments	NA	9	1.778	16	24	384
601.27(c); Request for full or partial waiver of safety and effectiveness assessments	NA	8	1	8	8	64
601.70(b) and (d), and 601.28; Annual progress reports of postmarketing studies	2252	101	1.84	186	24	4,464
610.15(d); Request for exceptions or alternatives to the regulation for constituent materials	NA	1	1	1	1	1
680.1(c); Requirement to annually update a license file with the list of source materials and the suppliers of the materials	NA	9	1	9	2	18
680.1(b)(3)(iv); Requirement to notify FDA when certain diseases are detected in source materials	NA	1	1	1	2	2
601.12; Amendments/Resubmissions	356h	170	27.888	4741	20	94,820
Section 402(j)(5)(B) of the PHS Act; Certification to accompany biological product applications	3674	1,291	1	1,291	0.28 (17 minutes)	358
Total						907,806

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] The numbers in this column have been rounded to the nearest whole number.

Table 2.--Estimated Annual Third-Party Disclosure Burden[1]

21 CFR Section; Activity	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours[2]
601.6(a); Requirement to notify selling agents and distributors upon suspension of license	1	20	20	0.33 (20 minutes)	7

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] The number in this column has been rounded to the nearest whole number.

Our estimated burden for the information collection reflects an overall increase of 467,907 hours and a corresponding increase in responses. Most of our adjustment reflects an increase in the number of annual submissions that we have received under §§ 601.12(b)(1) and (3), (e), and (f)(4), and 601.45 over the last few years. We attribute the remaining increase (358 hours) to submissions of Form FDA 3674.

Dated: February 15, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023-03508 Filed: 2/17/2023 8:45 am; Publication Date: 2/21/2023]