

UNITED STATES FOOD AND DRUG ADMINISTRATION

Survey of Drug Product Manufacturing, Processing, and Packing Facilities

OMB Control No. 0910-NEW

SUPPORTING STATEMENT

Part A: Justification

1, Circumstances Making the Collection of Information Necessary

Background

This section provides background on the Current Good Manufacturing Practices (CGMP) legislation for drug product manufacturing, processing and packing facilities (21 CFR Part 210 and 211), the objectives of this survey, and an overview of data collection methods.

This is a one-time information collection, the primary purpose of which is to collect industry-wide data on how facilities that manufacture, process and pack drug products for use in humans and/or animals ensure the quality of their operations, including their current risk management approaches and practices for ensuring the quality and suitability of the drug components, containers, and closures that they use. The data collection will involve administering a multi-mode survey to a randomly selected, representative sample of facilities involved in the manufacture, packing, repacking, labeling, relabeling, sterilizing, or testing of prescription or over-the-counter domestically- or foreign-produced drug products that are sold in the United States for use in humans or animals. The survey will assess current risk management approaches and practices in use for ensuring quality and suitability of drug product components and drug product containers and closures.

FDA intends to use this information to inform its economic analyses of potential updates to CGMPs for human and animal drug product manufacturing, processing and packing facilities under 21 CFR Parts 210 and 211.

Need and Legal Basis

The following regulations enable a common understanding of the regulatory process by describing the requirements to be followed by drug product manufacturing, processing and packing facilities and FDA:

- **21 CFR Part 210** - Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs, General.
- **21 CFR Part 211** - Current Good Manufacturing Practice for Finished Pharmaceuticals.

FDA has the responsibility to regulate the safety, as well as the efficacy and quality, of drugs in the United States. Under the FDA Safety and Innovation Act of 2012 (FDASIA), the term CGMP includes the implementation of oversight and controls over the manufacturing, processing and packing of drugs to ensure quality, including managing the risk of, and establishing the safety of, raw materials used in the manufacture of drugs. The safety and availability of drugs can be affected by raw material suppliers, the material supply chain, and the facility's controls over raw material quality. Risk management enables manufacturers to make proper choices and ensure the continued suitability of these materials and supply chains. Thus, the Agency would like to better understand how manufacturers, processors, and packers of drug products approach managing risks related to components, containers, and closures as well as the supply and distribution chains between the producers of raw materials and drug product manufacturers, processors, and packers. Such information will allow FDA to examine the potential economic impact of changes to regulations that govern the manufacturing, processing, and packing of drugs.

2. Purpose and Use of the Information Collection

The objectives of this information collection are to: (1) collect data establishing the current baseline risk management approaches and practices for qualification and oversight of suppliers of drug product components, containers, and closures used in the manufacturing, processing, and packing of drug products for the United States market (including those that produce and ship into the U.S. market from foreign countries); (2) acquire baseline data on current practices to facilitate comparisons with updated current good manufacturing practices concerning supply chain risk management procedures, including component risk evaluations, the number and frequency of supplier audits, and sampling and testing of components, containers, and closures; (3) collect baseline data on quality management practices, such as stability testing and expiration dating; and, (4) collect information on the types of water used by drug product manufacturers, processors, and packers during their processes.

The results of this information collection will (1) enhance FDA's CGMP compliance assistance to drug product manufacturers, processors and packers; and (2) determine what current practices are throughout this industry that can be used as a baseline for FDA's economic analyses when considering any potential proposed updates to CGMP standards.

3. Use of Information Technology and Burden Reduction

Respondents will be encouraged to submit the survey online, although a paper version will also be made available to respondents. presents how FDA plans to administer the survey.

Table 1. Mixed-mode Survey Protocol with Multiple Contacts

Contact	Contact Type	Content
Initial Contact	Email	Survey Pre-notification/Survey Link
First Reminder	Email and Mail	Survey Reminder with Survey Link/Survey Reminder Cover Letter with Hardcopy Survey (2 weeks after initial contact)
Second Reminder	Email and Mail	Survey Reminder with Survey Link and Reminder Postcard (2 weeks after first reminder)
Third Reminder	Email and Mail	Survey Reminder with Survey Link/Survey Reminder Cover Letter with Hardcopy Survey (1 week after second reminder)
Fourth Reminder	Telephone	Survey Reminder/Caller Offers to Issue Survey by Phone (1 week after second reminder)

All respondent facilities in the survey sample will be e-mailed a brief pre-notification letter from FDA explaining the nature and purpose of the survey and providing them with their unique password and the survey URL (Initial Contact). After two weeks, non-responders will receive a reminder email with their unique password and the survey URL and a reminder via USPS that includes a cover letter, a hard-copy of the survey, and a return envelope (First Reminder). The cover letter will urge them to log onto the online survey but will note that they could mail the hard-copy survey via USPS in the return envelope provided if they so choose. After another two weeks, non-responders will receive another email with their unique password and the survey URL and a reminder postcard via USPS (Second Reminder). One week after that, non-responders to date will receive another reminder email with their unique password and the survey URL and a reminder mailing via USPS that includes a cover letter, a hard-copy of the survey, and a return envelope (Third Reminder). Approximately a week after the third reminder, remaining non-responders will be contacted by telephone and offered the opportunity to do the survey over the phone.

Considering that the respondent population comprises technologically up-to-date businesses, FDA is hopeful for at least 80 percent of responses to be submitted electronically. The online survey software eliminates the respondents' burden of following the paper survey's skip patterns, as the software follows the skip patterns automatically, thus eliminating a potential source of respondent error. The online survey will also have explanatory mouse-over pop-up balloons that explain some terms identified as potential frequently asked questions (FAQs). This feature, while impractical to include fully in the paper survey, can reduce the need for calls to the survey

helpline and thus reduce respondent burden. It also saves respondents' time by eliminating the need to refer back to a separate Glossary section that is included with the paper survey. There will also be a dedicated email address to which respondents will be able to submit their questions.

4. Efforts to Identify Duplication and Use of Similar Information

This information collection does not duplicate any other effort. A comprehensive review of academic and trade literature did not identify any data collection on drug product manufacturing, processing and packing practices that can be used in economic analyses of potential updates to CGMP regulations.

5. Impact of Small Businesses or Other Small Entities

The survey sample will include small businesses, which, for “Pharmaceutical Preparation Manufacturing” (NAICS 325412) and “Biological Product (except Diagnostic) Manufacturing” (NAICS 325414), the Small Business Administration (SBA) defines as those firms with fewer than 1,250 employees (SBA, 2017). Their burden is minimized because the online survey, which we expect most targeted facilities to use, accommodates interruptions, i.e., respondents can close the survey web page and return to where they left off simply by logging on again. Further, the majority of survey questions are closed-ended questions; only two questions ask the respondents for verbatim, open-ended answers. Also, there will be a toll-free helpline number to call if facilities have questions about their survey eligibility or any other aspect of the survey. In addition, some small businesses will not be in-scope because they are not drug product manufacturers, processors or packers. These small businesses will be screened out after answering just seven demographic questions about their facility size and main line of business.

6. Consequences of Not Collecting the Information Less Frequently

Failure to obtain the data provided by this collection will adversely impact FDA's ability to conduct a thorough analysis of the economic impacts of potential updates to CGMP standards in the drug product manufacturing, processing and packing industry. Failure to collect this information may also impede FDA's efforts to demonstrate current drug industry practices and develop and issue documents, including regulations, that would most benefit facilities with their CGMP practices.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances associated with this collection of information.

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

FDA published a 60-day notice for public comment in the *Federal Register* of September 18, 2020 (85 FR 58370). Although one comment was received, it was not responsive to the four collection of information topics solicited and therefore will not be discussed in this document.

9. Explanation of Any Payment or Gift to Respondents

There will be no payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

Survey respondents will be de-identified through the use of randomly-assigned respondent ID numbers, which will also be their usernames for the online survey. No one outside the FDA contractor's survey team will have access to the individual survey responses, nor will the contractor's survey team provide to FDA or to anyone else outside the survey team any information that enables identification of any individual facility or company with their responses. We will not collect any personal identifiable information with this survey. All covered information will be maintained in password-secured files on the contractor's internal server (i.e., only members of the contractor's survey team will have access to the files). The contractor's internal servers are protected by Sonic firewall, and the servers are housed in a locked room accessible only to IT staff.

The printing and mailing tasks associated with the survey (i.e., notification letters, reminder letters, and envelopes) will be performed by the FDA contractor's survey team.

The on-line surveys will be hosted by Qualtrics. Their software uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. Qualtrics will also protect surveys with passwords (provided by the survey team) and HTTP referrer checking. Qualtrics services are hosted by trusted data centers, which are independently audited using the industry standard SSAE-16 method, to ensure the highest protection, per HITECH requirements. Qualtrics deploys the general requirements set forth by several federal Acts, including the FISMA Act of 2002, and meets or exceeds the minimum requirements as outlined in FIPS Publication 200.

Undeliverable survey-related letters will be returned directly to the FDA by the U.S. Postal Service. FDA will then forward all unopened undeliverable mailings to its survey contractor.

For surveys submitted by mail, members of the FDA contractor's survey team will open them and enter the data into Qualtrics. Only assigned team members will be able to crosswalk respondents' names with their usernames. All assigned team members will have acknowledged and signed the required Code of Business Conduct and Ethics, which (among other things)

requires them to maintain the integrity, confidentiality, and accuracy of all data and information obtained during the course of this data collection effort. At the end of the survey, the contractor team will ensure the proper storage and/or destruction of all data in compliance with all relevant government regulations and policies.

11. Justification for Sensitive Questions

No questions of the type commonly considered to be “sensitive” are asked by this survey. However, FDA acknowledges that some respondents may consider questions regarding facility size and revenue sensitive. The survey asks respondents to answer the following questions:

- The number of employees that work at the facility (one of four ranges can be selected),
- The number of employees at the parent company (one of two ranges can be selected), and
- The parent company’s gross revenue in the last fiscal year (one of seven ranges can be selected).

Facility and firm size and revenue data are readily available from other information sources, such as the DUNS database, but it is best survey practice to request these data as the survey is administered to ensure up to date information. To mitigate any potential sensitivity, FDA’s contractor maintains the privacy of all respondents’ survey responses, as described in B.10.

12. Estimates of Annualized Burden Hours and Cost

12a. Annualized Hour Burden Estimates

For the survey, the estimated number of respondents reflects the planned sample of 1,396 facilities that could potentially choose to take the survey (and thus incur a response burden). Calculation of the number of survey completions—754—is based on a response rate of 60 percent and an estimate of 10 percent sampling frame deficiency (i.e., $(1,396 * .60) * (1 - .10) = 754$), as described in Statement B. However, the calculation of the burden presented below is based on the highly conservative, extreme-case assumption that all 1,396 targeted facilities in the sample will complete the survey instead of the 754 we expect to respond.

The burden hour estimate for an average facility to complete the survey is based on tests of the length of time each type of respondent is likely to need to read the survey invitation and instructions and complete the survey questions. For facilities engaged in drug product manufacturing (in addition to other possible activities) in the U.S., this burden was estimated as 6 minutes to read instructions and 60 minutes to answer questions. The burden in hours for facilities engaged in other forms of drug processing or packing (non-manufacturers) was estimated at about 70 percent of the burden to drug product manufacturers.¹ Many of these

¹For the purposes of the survey to distinguish operations that manufacture drugs from other operations, we

facilities will skip past sections of the survey directed only toward facilities that manufacture drug products. Given the language barrier, the burden for facilities outside of the U.S. was estimated at double that of domestic facilities.

The current collection activities are expected to be initiated and completed within one calendar year; therefore, Table 2 can be considered an “annual” burden estimate for the one calendar year in which burden would be realized.

Table 2. Estimated Annual Reporting Burden¹

Type of Facility	Number of Total Respondents	Number of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Burden
Group 1: Facilities in U.S. engaged in drug product manufacturing (in addition to other possible activities)	394	1	394	1.10	433
Group 2: Facilities in U.S. not engaged in manufacturing but engaged in other forms of drug processing or packing (e.g., labeling, repacking, etc.)	333	1	333	0.75 (45 min.)	250
Group 3: Facilities outside U.S. engaged in drug product manufacturing (in addition to other possible activities)	407	1	407	2.20	895
Group 4: Facilities outside U.S. not engaged in manufacturing but engaged in other forms of drug processing or packing (e.g., labeling, repacking, etc.)	261	1	261	1.50	392
Total	1,396	1	1,395	1.41	1,970

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

12b. Annualized Cost Burden Estimate

The wages used for survey respondents reflect the median hourly wage for top executives and managers in the pharmaceutical manufacturing industry in the United States (BLS, 2018a). The survey respondents are likely to be managers of the regulatory affairs, quality control, or production departments at surveyed facilities, or higher-level executives of small- to medium- collectively refer to the following activities as *drug processing and packing*: analysis, analytical testing, labeling, packing, relabeling, and repacking and sterilizing.

sized companies. We calculated an hourly labor cost to employers based on the ratio of total benefits to wages and salaries for the 90th wage percentile in private industry (see Table A, *Employer Costs for Employee Compensation by Wage Percentile, March 2019*, in BLS, 2019). BLS reported that total benefits were \$21.96 for a wage of \$46.64 per hour, which is the 90th wage percentile in private industry. Benefits thus amounted to approximately 47 percent of the 90th percentile wage. Therefore, the actual hourly wages for potential respondents, as reported by BLS (2018a), was multiplied by 1.47 to reach the “wages plus benefits” figures used to compute the overall burden in dollars. We did not adjust the wage estimate for foreign survey respondents. While the U.S.-based wage estimate may be appropriate for those targeted respondents in highly developed countries, such as Germany, Japan, and the U.K., it may overestimate those in developing nations, such as India and Pakistan.

The total annual burden cost is calculated by the estimated annual burden hours times 1.47 times the median hourly wage rate for the pharmaceutical company executives and managers considered likely to be the people filling out the survey (see Table 3). For this estimate, it is assumed that half the survey completions will be by managers and half by top executives.

Table 3. Estimated Respondent Burden Cost [a]

Type of Respondent	Median Hourly Wage Rate	Average Benefits (47% of Median Hourly Wage)	Median Hourly Wage Rate Including Benefits	Average Burden per Response (in hours)	Average Cost per Response	Estimated Total Burden Cost
Group 1: Facilities in U.S. engaged in drug product manufacturing (in addition to other possible operations)						
General & Operations Managers	\$68.05	\$31.98	\$100.03	1.10	\$110.03	\$21,676 ^[b]
Senior executives	\$71.17	\$33.45	\$104.62	1.10	\$115.09	\$22,673 ^[b]
Group 2: Facilities in U.S. not engaged in manufacturing but engaged in other forms of drug processing or packing (e.g., labeling, repacking, etc.)						
General & Operations Managers	\$68.05	\$31.98	\$100.03	0.75	\$75.02	\$12,453 ^[c]
Senior executives	\$71.17	\$33.45	\$104.62	0.75	\$78.47	\$13,104 ^[c]
Group 3: Facilities outside U.S. engaged in drug product manufacturing (in addition to other possible operations)						
General & Operations Managers	\$68.05	\$31.98	\$100.03	2.20	\$220.07	\$44,674 ^[d]
Senior executives	\$71.17	\$33.45	\$104.62	2.20	\$230.16	\$46,953 ^[d]
Group 4: Facilities outside U.S. not engaged in manufacturing but engaged in other forms of drug						

Type of Respondent	Median Hourly Wage Rate	Average Benefits (47% of Median Hourly Wage)	Median Hourly Wage Rate Including Benefits	Average Burden per Response (in hours)	Average Cost per Response	Estimated Total Burden Cost
processing or packing (e.g., labeling, repacking, etc.)						
General & Operations Managers	\$68.05	\$31.98	\$100.03	1.50	\$150.05	\$19,507 ^[e]
Senior executives	\$71.17	\$33.45	\$104.62	1.50	\$156.93	\$20,558 ^[e]
Total						\$201,598

Sources: BLS 2018a; BLS, 2019

^[a] Totals may not sum and calculations may produce different results due to rounding and truncated inputs.

^[b] Assumes 197 Managers and 197 Executives responding for a total of 394 targeted drug product manufacturer respondents.

^[c] Assumes 166 Managers and 167 Executives responding for a total of 333 targeted other drug product processors.

^[d] Assumes 203 Managers and 204 Executives responding for a total of 407 targeted drug product manufacturer respondents.

^[e] Assumes 130 Managers and 131 Executives responding for a total of 261 targeted other drug product processors.

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

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The cost of this information collection effort to the Federal government is provided in Table 4. Subject to OMB approval, the survey is expected to be fielded in late 2021. Preparations have been underway since late 2017, including survey design and writing, obtaining data on facilities in the survey universe, survey website design, and preparation of outreach materials.

Table 4. Cost to the Federal Government [a]

Activity	Year 1 (2017)	Year 2 (2018)	Year 3 (2019)	Year 4 (2020)	Year 5 (2021) ^[b]	Total (2017-2021)
Government Activity [c]						
Reviewing and	\$14,973	\$48,661	\$51,094	\$53,649	\$54,165	

Activity	Year 1 (2017)	Year 2 (2018)	Year 3 (2019)	Year 4 (2020)	Year 5 (2021) ^[b]	Total (2017-2021)
providing guidance on instruments, OMB clearance, and data collection approach						\$222,542
Contractor Activity^[d]						
Survey Instrument Development and Sampling Design	\$7,466	\$22,359	\$35,568	\$0		\$65,393
Information Collection Request for OMB			\$16,450			\$16,450
Survey Administration				\$97,129		\$97,129
Survey Data Analysis and Reporting					\$64,917	\$64,917
Total	\$7,466	\$22,359	\$52,018	\$97,129	\$64,917	\$243,889

^[a] Totals may not sum, and calculations may produce different results due to rounding and truncated inputs.

^[b] Current period of performance ends December 17, 2021.

^[c] Assumes a single GS-14 staff. According to national industry-specific occupational employment and wage estimates (BLS, 2018b), social scientist and related workers in “Management, Scientific, and Technical Consulting Services” (NAICS 541600) on average earned \$47.25 in 2018, which is approximately \$66.15 including benefits ($\$47.25 * 1.47$). https://www.bls.gov/oes/current/naics4_541600.htm#19-0000

^[d] Consists of contractor costs estimated at \$103.34 per hour on average, including labor and overhead charges.

15. Explanation for Program Changes or Adjustments

This is a new information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Planning for the survey started in November 2017. All survey-related activities will be completed within one year of OMB approval. The anonymized, aggregated results of the survey will be made available by the contractor to FDA. The findings from the survey will be summarized and analyzed in a report from the contractor to FDA.

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

The expiration date will be displayed on all letters to the respondents and on each web page of the survey.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

References

Bureau of Labor Statistics (BLS). (2018a). May 2018 National Occupational Employment and Wage Estimates. NAICS 325400 - Pharmaceutical and Medicine Manufacturing. Available at https://www.bls.gov/oes/current/naics4_325400.htm#11-0000.

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