U.S. Food & Drug Administration

Obtaining Information for Evaluating Nominated Bulk Drug Substances for Use in Compounding Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.

OMB Control No. 0910-NEW

SUPPORTING STATEMENT—**Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, us or we) research. Section 503B of the Federal Food, Drug and Cosmetic Act (FD&C Act) describes the conditions under which outsourcing facilities, a new type of drug compounder established in 2013, may be exempt from the following requirements of the FD&C Act: requirements for FDA approval of drugs in section 505 of the FD&C Act (21 U.S.C. 355), labeling with adequate directions for use under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)), and drug supply chain security requirements under section 582 (21 U.S.C. 360eee-1).

One of the conditions that must be met for a drug product compounded by an outsourcing facility to qualify for these exemptions is that the outsourcing facility may not have compounded a drug using a bulk drug substance unless (1) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need ("*bulks list*"); or (2) the substance appears on the drug shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing.

FDA has solicited nominations for the 503B bulks list and has received over 200, but these these nominations often do not contain substantive information on the current and historical use of these substances in clinical practice to inform FDA's evaluation. Developing the 503B bulks list is a significant priority for the agency. To inform our evaluation of bulk drug substances for inclusion on the 503B bulks list, we have entered into research studies with the University of Maryland (UMD) Center of Excellence in Regulatory Science and Innovation (CERSI) and the Johns Hopkins University (JHU) CERSI. We intend to seek input from the UMD-CERSI and JHU-CERSI on the use of these bulk drug substances in clinical practice by examining their current and historical use in compounding.

We therefore request OMB approval of the information collection as discussed in our supporting statement parts A and B.

2. Purpose and Use of the Information

Information regarding the historical and current use of the substances in compounding obtained by this research will help inform our assessments as to the clinical need for outsourcing facilities to compound drug products using nominated bulk drug substances. We intend to use a two-part analysis in evaluating substances nominated for placement on the 503B bulks list to determine

whether there is a clinical need. The collaboration with UMD-CERSI and JHU-CERSI pertains to Part 2 of the analysis, which applies to bulk drug substances that are not components of FDA-approved drug products, as well as certain bulk drug substances that are components of FDA-approved drug products and that have gone through Part 1 and warrant further evaluation under Part 2 of the analysis. One of the factors that FDA considers under Part 2 is "current and historical use of the substance in compounded drug products, including information about the medical condition(s) that the substance has been used to treat and any references in peer-reviewed medical literature."

Information regarding the historical and current use in clinical practice of compounded drugs containing these bulk drug substances obtained by UMD-CERSI and JHU-CERSI will help inform FDA's assessments as to the clinical need for outsourcing facilities to compound drug products using the bulk drug substances.

3. Use of Information Technology and Burden Reduction

Researchers may use interviews, focus groups, and questionnaires, as appropriate, to obtain information concerning the use of compounded drug(s) from medical experts, outsourcing facilities, and other stakeholders. Web-based data collection tools will be used for questionnaires to minimize respondent burden.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of a similar data collection.

5. Impact on Small Businesses or Other Small Entities

We expect most respondents will be private individuals.

6. Consequence of Collecting the Information Less Frequently

The proposed data collection is a discrete endeavor relevant to the specific study described.

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

There are no special circumstances for this collection of information.

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

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the Federal Register of September 17, 2018 (83 FR 46957). One comment was received, however it pertained to a different docket and we have posted the comment to the appropriate docket accordingly.

9. Explanation of Any Payment or Gift to Respondents

No payments or gifts will be provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

Information provided by respondents will be kept private and anonymous, except as otherwise required by law. All information that can identify individual respondents will be kept by FDA's UMD CERSI and JHU CERSI partners in files that are separate from information provided to FDA.

Respondents also will be advised of the following: the nature of the activity; the intended purpose and use of the data collected; FDA sponsorship; and the fact that participation is voluntary at all times.

The UMD CERSI research study was found to be exempt from the "*Regulations for the Protection of Human Subjects*" requirements in accordance with paragraph b(2) of 45 CFR Sec. 46.101 by the Research Involving Human Subjects Committee (RIHSC). As necessary, the JHU CERSI study methods will be evaluated by RIHSC prior to information collection.

11. Justification for Sensitive Questions

This data collection will not include sensitive questions. The complete list of questions is Included with our supporting statement part B.

12. Estimates of Annualized Burden Hours and Costs

12a. Estimated Annualized Hourly Burden

UMD-CERSI researchers will study the current and historical use of 75 bulk drug substances per year. FDA estimates that each bulk drug substance may have uses that relate to, on average, two different medical specialties, yielding 150 bulk drug substance-specialty combinations. We estimate a total of 15 different specialties will be implicated and therefore that 10 bulk drug substance uses will be relevant to each specialty on average (150/15).

For focus groups and interviews, UMD-CERSI will seek to include around 10 experts from each of the 15 specialty groups, yielding a total of 150 respondents. Each respondent will opine on each of the 10 bulk drug substance uses that are relevant to their specialty, yielding an estimated 1,500 annual responses. The average burden per response is 2 hours, for a total of 3,000 annual burden hours.

For the expert questionnaire, we estimate UMD-CERSI will obtain responses from 50 experts from each of the 15 specialty groups, yielding a total of 750 respondents. Each respondent will respond to a questionnaire on each of the 10 bulk drug substance uses that are

relevant to their specialty, yielding an estimated 7,500 annual responses. The average burden per response is 30 minutes, for a total of 3,750 annual burden hours.

JHU-CERSI will study the use of six bulk drug substances in patients with autism spectrum disorder (ASD) and will use a questionnaire to obtain information from parents on the use of these substances. Researchers will seek responses from 1,000 parents of children with ASD. The average burden per response is 30 minutes, for a total of 500 annual burden hours.

FDA therefore estimates the burden of this collection of information as follows:

Table 1. Estimated Annual Reporting Burden

Information Collection	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
UMD-CERSI Expert focus groups and interviews	150	10	1500	2	3,000
UMD-CERSI Expert questionnaire	750	10	7,500	.5	3,750
JHU-CERSI Parent questionnaire	1,000	1	1,000	.5	500
TOTAL	1,900		10,000		7,250

12b. Annualized Cost Burden Estimates

We estimate no capital costs to respondents for the collection of information.

13. Estimates of Other Total Annual Cost Burden to Respondents or Recordkeepers

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

14. Annualized Cost to the Federal Government

The total estimated cost to the Federal Government for the collection of data is $737,198; with an annual cost to FDA of $29,000. This includes the costs paid to UMD CERSI and JHU CERSI grantees to obtain the information described in this collection, assess results, and prepare a report ($650,198). The cost also includes FDA staff time to provide information and feedback to UMD and JHU CERSI, including identifying specific bulk drug substances for inclusion in the study ($87,000; 4 hours per week for 3 years).

15. Explanation for Program Changes or Adjustments

This is a new information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Assessment of the information collected will be primarily qualitative (for example, content analysis for in-depth interviews); some quantitative analysis will be conducted for information obtained through questionnaire instruments.

FDA will receive summarized research results from grantees on a rolling basis beginning 10 months after project initiation. Research results will be made publicly available. The UMD-CERSI research is expected to last three years and the JHU-CERSI research is expected to last one and a half years.

Please see Supporting Statement B for additional description of research methods.

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

The OMB expiration date will be displayed on the collection instruments.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.