Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies

OMB Control No. 0910-0119

SUPPORTING STATEMENT Part A

A. Justification

1. Circumstances Making the Collection of Information Necessary

Sections 402, 406, 408, 409, 501, 502, 503, 505, 510, 512-516, 518-520, 571, 701, 721, 801, 905, 910, and 911 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and sections 351 and 354-360F of the Public Health Service Act require sponsors or manufacturers of certain Food and Drug Administration (FDA)-regulated products (e.g., food and color additives, animal food additives, human and animal drugs, devices, biological products, electronic products, and tobacco products) to demonstrate the safety and effectiveness of their product in applications or submissions to FDA prior to marketing those products or prior to allowing certain products into clinical studies. Such applications and submissions contain, among other important items, full reports of all nonclinical laboratory studies done to demonstrate product safety in man and/or other animals. In order to ensure the quality and integrity of the data from these nonclinical laboratory studies, the agency issued good laboratory practice (GLP) regulations for nonclinical laboratory studies in part 58 (21 CFR part 58).

In the Federal Register of August 24, 2017 (81 FR 58342) FDA published a proposed rule to amend the GLP regulations in part 58 to require a complete quality system approach, referred to as a GLP Quality System, when safety and toxicity studies support or are intended to support applications or submissions for products regulated by FDA. If finalized, the rule will expand the scope of the GLP regulation to include all products for which nonclinical laboratory studies are currently conducted that are not explicitly discussed in the current regulation, specifically tobacco products. The proposed expanded scope also includes all applications and submissions under the FD&C Act that can be supported by the results of nonclinical laboratory studies.

As discussed in the proposed rule, provisions for reporting and recordkeeping presently required by 21 CFR part 58, Good Laboratory Practice for Nonclinical Laboratory Studies would be revised to support the new regulatory requirements. Accordingly, FDA is requesting OMB approval for the information collection provisions associated with its proposed rule.

2. Purpose and Use of the Information Collection

Results of nonclinical laboratory studies may be submitted in support of applications and submissions to FDA by persons desiring to market new products or research such products in clinical studies. The information submitted to FDA surrounding a nonclinical laboratory study, such as the final study report, gives FDA's scientific review experts the information needed to help determine the safety or toxicity of the test article or both. FDA uses such safety and toxicity information to make regulatory decisions regarding the test article, including permitting the conduct of clinical studies on human subjects, determining safe levels of residual drug for drugs

administered to animals whose products will be consumed by humans, and marketing new products for both human and non-human animal use.

FDA's regulations in part 58 require testing facilities engaged in conducting nonclinical laboratory studies to retain, and make available to regulatory officials, records regarding compliance with good laboratory practices. Recordkeeping is necessary to document the conduct of nonclinical laboratory studies of FDA-regulated products to ensure the quality and integrity of the resulting final study report on which a regulatory decision may be based. FDA conducts on-site reviews of records and reports during inspections of persons conducting one or more nonclinical laboratory study phases and uses the information to verify the reliability of results submitted in support of applications and submissions to FDA.

3. Use of Improved Information Technology and Burden Reduction

FDA estimates that 90% of the respondents will use electronic means to fulfill the agency's requirement or request. FDA, as an agency, is aware of the dramatic cost improvements possible through computerization and is actively encouraging electronic recordkeeping and electronic submission of new product applications. FDA is proposing to update part 58 to help address the use of present technology. Currently, some provisions, which were written prior to the widespread use of electronic media, require persons conducting nonclinical laboratory studies to maintain paper records, requirements that hamper the efficient use of resources. However, this proposal would modernize our regulations to allow for the acceptance of electronic records rather than requiring paper records. In addition, we propose eliminating any current requirements that might impede a fully computerized facility.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

As discussed in the Preliminary Regulatory Impact Analysis (PRIA), the Small Business Administration (SBA) uses different definitions of small entity for different industries. Based on SBA size standards, except for blood and organ banks whose size is determined based on revenues, most firms covered by the proposed rule would be considered small if they employ fewer than 500 employees. Firms in the tobacco industry would be considered small if they employ fewer than 1000 employees. Firms in the pharmaceutical industry are considered small if they employ fewer than 750 employees. Blood and organ banks would be considered small if their annual revenue is less than $10 million.

Currently available data from the 2007 Economic Census show that at least 92 percent of the establishments in pharmaceutical, medical devices, foods, and biologics (except blood and blood organs) industries would be considered small by SBA standards. Our Registration and Listing data indicate that 15 (12.7 percent) of the registered tobacco manufacturers are considered small. Using revenue measures as determined by the SBA standards we estimate that 72 percent of blood and organ banks would be considered small. The proposed procedures are no more

burdensome for small businesses than for large. The proposed recordkeeping requirements are the minimum requirements to ensure documentation of the conduct and data collection of nonclinical laboratory studies of FDA-regulated products and thus ensure the quality and integrity of the resulting final study report. The proposed regulations provide flexibility to entities involved in the conduct of nonclinical laboratory studies, including the sponsor, testing facility, and any contracted persons. This provides the necessary flexibility to accommodate the various methods and capabilities of both large and small entities. FDA aids small businesses in complying with its requirements through the agency's Regional Small Business Representatives and through the scientific and administrative staffs within the agency. FDA has provided a Small Business Guide on the agency's website at http://www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm.

6. Consequences of Collecting the Information Less Frequently

Information collection schedule is consistant with regulatory requirements and requires reporting only on an occasional basis. We believe this imposes minimal burden on respondents while at the same time preserving data quality of information submitted to the agency.

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

The subject information collection requirements are consistent with 5 CFR §1320.5 with the exception of the 5-year retention of records related to nonclinical laboratory studies supporting investigational new drug applications (INDs) or applications for investigational device exemptions (IDEs). This extended retention period is necessary because it is approximately a 5-year process. These records must be available to FDA inspectors so they can be examined during on-site visits to verify the quality and integrity of the data.

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

As required by section 3506(c)(2)(B) of the Paperwork Reduction Act of 1995 (PRA), FDA provided an opportunity for public comment on the information collection requirements of the proposed rule that published in the Federal Register on August 24, 2016 (81 FR).

In addition, FDA published an advanced notice of proposed rulemaking entitled, "*Good Laboratory Practice for Nonclinical Laboratory Studies*" (75 FR 80011, December 21, 2010), to solicit stakeholder input regarding FDA's intention to modify the GLP regulations in part 58. All comments were reviewed and considered by a working group with representatives from all FDA Centers, along with representatives from the U.S. Environmental Protection Agency (EPA), the Animal and Plant Health Inspection Service of the U.S. Department of Agriculture (USDA/APHIS), and the Office of Laboratory Animal Welfare at the National Institutes of Health (NIH/OLAW).

Finally, FDA has extensive contacts and consults with the affected industry, other government agencies, and international organizations which have an interest in the

implementation of the GLP regulations. The regulations have been revised four times since their inception in 1978, to refine and improve their application. These consulting efforts continue.

9. Explanation of Any Payment or Gift to Respondents

FDA does not provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Information submitted to FDA may contain trade secret and confidential commercial information. In addition, the agency expects that it may inspect firm records containing confidential commercial information. Only information that is releasable under the agency's regulations in 21 CFR part 20 would be released to the public. This information is also safeguarded by Section 301(j) of the FD&C Act and would be protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)). To the extent 21 CFR 20.64 applies, FDA will honor the confidentiality of any data in investigation records compiled for law enforcement purposes. All records and reports maintained by FDA are kept in limited access areas.

11. Justification for Sensitive Questions

The information collection does not contain questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

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

Description of respondents: Respondents to the information collection are persons conducting a phase of a nonclinical laboratory study that is within the proposed expanded scope of part 58, including their personnel, independent contributing scientists, and study sponsors as the latter two terms are defined in this proposed rule; universities; or government agencies.

Reporting:

Currently, the GLP regulations include: (1) Report the results of QAU inspections; (2) submit periodic QAU study reports; (3) provide a QAU statement as part of the final study report; (4) provide the results of test and control article characterization and the testing of mixtures of test and control articles with carriers; (5) report a change in archive location; and (6) prepare in writing a final study report containing an overall interpretation of nonclinical laboratory studies.

The proposed rule will revise these requirements to include (1) a final study report incorporating additional information about all persons conducting one or more nonclinical laboratory study phases and a study director's compliance statement; (2) QAU reports on facility-based inspections and process-based inspections, where conducted; (3) written certification whenever a process-based QAU inspection reveals problems, with documentation that records the actions taken; (4) summaries of the close-out of discontinued studies; (5) notification of the change of archival site within a specified timeframe; (6) reports by the study sponsor to the study director of known risks of the test article and necessary measures to protect study personnel; and (7) reports by the study sponsor to the study director of the results of characterization of any reference articles that may be employed in a study as well of mixtures of such reference articles with carriers. Finally, for sponsors who submit the results of nonclinical laboratory studies in support of applications or submissions to FDA that are proposed additions to the scope of part 58 and that lack enacting regulations, (8) submission of the final study report and a GLP compliance statement.

QAU inspection reports provide the study director and management with executive responsibility information about the progress of a study and its compliance with GLP regulations so they can take any corrective actions required to ensure the quality and integrity of the data. Test, control, and reference article information helps ensure proper dosing of the test system(s) and allows interpretation of study results in the final study report. The study sponsor receives the final study report and commonly submits the report in support of an application or submission to FDA. The information in the final study report gives FDA's scientific review experts the information needed to help determine the safety or toxicity of the test article or both. FDA needs such safety and toxicity information to make regulatory decisions regarding the test article, including permitting the conduct of clinical studies on human subjects, determining safe levels of residual drug for drugs administered to animals whose products will be consumed by humans, and marketing new products for both human and non-human animal use. Since a number of the additional applications and submissions proposed for the scope expansion do not have enacting regulations, inclusion in part 58 is necessary.

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

Table 1.—Estimated One-time Reporting Burden[1]

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
Read and Understand the Proposed Rule: Sponsors of Nonclinical Laboratory Studies	2,193	1	2,193	7.2	15,790
Read and Understand the Proposed Rule: Testing Facilities of Nonclinical Laboratory Studies	300	1	300	18	5,400
Total			2,493		21,190

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

Table 1 shows the estimated one-time burden associated with the new reporting provisions of the proposed rule. We expect that persons conducting a phase of a nonclinical laboratory study that is within the proposed expanded scope of part 58 will need to read and understand the

proposed rule. We expect that some entities would face lower complexity from reading the proposed rule and some entities would face higher complexity. In the PRIA, we calculated lower and upper estimates of time to read and understand the proposed rule under a low-complexity scenario for sponsors of nonclinical laboratory studies who would face fewer provisions. Our estimates under a high-complexity scenario apply to testing facilities of nonclinical laboratory studies that would have to read and understand more provisions in the rule. As stated in the PRIA, we estimate that there are 2,193 sponsors of nonclinical laboratory studies and 300 testing facilities of nonclinical laboratory studies. We estimate that the 2,193 sponsors of nonclinical laboratory studies will take from 4.8 to 9.6 hours, for an average of 7.2 hours, to read and understand the proposed rule. We expect that the 300 testing facilities of nonclinical laboratory studies will take from 12 to 24 hours, for an average of 18 hours, to read and understand the proposed rule.

Table 2 – Estimated Recurring Reporting Burden[1]

21 CFR Part 58	Number of respondents	Number of responses per respondent	Total annual responses	Avg. burden per response	Total hours
Proposed new requirements	300	224.9	67,465	1.03	69,386.25

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

Recordkeeping

Currently, the GLP regulations include requirements that respondents must record: (1) personnel job descriptions and summaries of training and experience; (2) master schedules, protocols, and protocol amendments; (3) equipment inspection, maintenance, calibration, and testing records; (4) SOPs; (5) documentation of feed and water analyses and animal treatments; (6) test article accountability records; and (7) study documentation, including raw data.

This proposed rule will add to the existing requirements with regard to initial changes and additions to SOPs for both testing facilities and test sites to develop, implement, and maintain a GLP Quality System and to expand many SOPs to specifically include multisite studies.

This proposed rule would also expand personnel record maintenance to require records of training and experience on GLP requirements and species-specific animal care. In addition, this proposed rule includes revisions to the required content of study protocols as part of a GLP Quality System and for multisite study specifics.

The additional documentation by management with executive responsibility and study directors is for the implementation of a GLP Quality System and the resulting additional burden is nominal. Documentation by independent contributing scientists, as defined in this proposed rule, includes records these individuals would usually retain, so nominal added burden is predicted.

To implement the proposed checks and balances discussed in the preamble to the proposed rule, proposed revisions will require that added documentation be made by study director and the QAU to ensure the viability of the proposed GLP Quality System (see Table 5).

This proposed rule also adds requirements for the study sponsor to maintain records of (1) protocol and protocol amendment approval; (2) the accreditation status of a contracted person (as defined in this proposed rule) that conducts a phase of the study that involves the use of animals; (3) test, control, and reference article characterization; and (4) the qualifications of all contracted persons.

In addition, the proposed rule includes recordkeeping requirements for nonclinical laboratory studies that choose to utilize the option of having a principal investigator, particularly for multisite studies. These individuals will have recordkeeping responsibilities comparable to those of the study director for the nonclinical laboratory study phases for which they are responsible.

The persons potentially retaining nonclinical laboratory study documents are persons conducting a phase of a nonclinical laboratory study that is within the proposed expanded scope of part 58, including independent contributing scientists, and study sponsors as defined in this proposed rule. Results of nonclinical laboratory studies may be used by firms in support of applications and submissions to FDA, including applications and submissions for research and marketing of new products. The additional documentation of the conduct and data collection of nonclinical laboratory studies of FDA-regulated products will help ensure the quality and integrity of the final study report. FDA conducts on-site reviews of records and study reports during inspections of persons conducting one or more nonclinical laboratory study phases to verify the reliability of results submitted in support of applications and submissions to FDA.

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

Table 3.—Estimated One-time Recordkeeping Burden[1]

Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Update Existing SOPs	300	12	3,600	7.5	27,000
Write New SOPs	300	10	3,000	24	72,000
Training	300	2	600	14	8,400
Total			7,200		107,400

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

Table 3 shows the estimated one-time burden associated with the revised recordkeeping provisions of the proposed rule. We expect that the 300 testing facilities of nonclinical laboratory studies will need to update existing SOPs and to write new SOPs. In the PRIA, we estimated that each facility would need to update 12 existing SOPs and write 10 new SOPs. We calculated lower and upper estimates of time to update existing SOPs and to write new SOPs. We estimate that it will take from 4 to 11 hours, for an average of 7.5 hours, to update 12 existing SOPs. We estimate that it will take from 15 to 33 hours, for an average of 24 hours, to write 10 new SOPs. We also expect that the 300 testing facilities of nonclinical laboratory studies will need to conduct training. In the PRIA, we estimated that for the low estimate one person would be doing the training and one person would be trained. By contrast, for the high estimate, we estimated that also one person would be doing the training and potentially three people would receive such training, for an average of two employees for each facility. We calculated lower and upper estimates of time to train, estimating that it will take from 5 to 23 hours, for an average of 14 hours, to train.

Table 4.—Estimated Recurring Recordkeeping Burden[1]

21 CFR Section Part 58	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. burden per recordkeeping	Total Hours
Proposed new requirements	300	20	1,188,031		906,289.5

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

With input from the Society for Quality Assurance (SQA) and other experts in the field, we estimated the number of entities (responders), the annual reporting frequency, and total labor hours associated with each of the additional proposed requirements.

12b. Annualized Cost Burden Estimate

Reporting Costs

The proposed rule proposes additional reporting responsibilities from various entities involved in the conduct of a nonclinical laboratory study to enhance the information that is essential to implement the proposed GLP Quality System, e.g., providing information on test, control, and reference article characterization, reporting results of process-based inspections, and adequate reporting of study deviations and study reports. Table 6A below briefly describes the additional reporting requirements, and the proposed entity responsible for ensuring the requirement is fulfilled.

Additional Reporting Responsibilities Proposed by the Rule	
Main Entity Responsible	Additional Reporting Responsibility
Sponsor	R01. Provide test, control, and reference article characterization and risk information
	R02. Provide nonclinical laboratory study report in support of applications and submissions
Quality Assurance Unit (QAU)	R03. Expanded content of QAU statement in final study report
Management with Executive Responsibility	R04. Management report of actions taken when a process-based inspection reveals problems
	R05. Management report of personnel deviations from protocol
Study Director	R06. Expanded contents of final study report
	R07. Compliance statement by study director appended to final study report
	R08. Summary report of close-out for discontinued studies
Contributing Scientists or Principal Investigators	R09. Reports by independent contributing scientist(s) to study director or principal investigator

	R10. Study deviation reports from principal investigator to study director
	R11. Signed and dated compliance statement, final study reports and amendments, if applicable, from principal investigator to study director
[1] Task may involve other assistance such as clerical.	

With input from the Society for Quality Assurance (SQA) and other experts in the field, we estimated the number of entities (responders), the annual reporting frequency, and total labor hours associated with each of the additional proposed requirements. In estimating the value of labor resources, we assume 25 percent of the total estimated labor time is allocated to clerical assistance. We seek comments or data to support other assumptions on this issue.

Because the composition of the entities affected cover manufacturers across all product areas regulated by FDA, we use the median hourly wage rate for industry sectors 31, 32, and 33 as reported by the Bureau of Labor Statistics for 2014 (Ref. 1) to value labor hours. Reporting responsibilities for the sponsor or other entities with a managerial role are valued using "Management Occupations," (Standard Occupation Code (SOC), 110000) at $52.80 per hour. Labor hours for contributing scientists or investigators are valued using an average of the wage rate for the following occupations "Statisticians" (SOC 152041, hourly wage of $45.71), "Chemists and Material Scientists" (SOC 192030, hourly wage rate of $35.82), "Veterinarians" (SOC 291131, hourly wage rate of $34.26), "Biochemists and Biophysicists" (SOC 191021, hourly wage rate of $40.92), "Environmental Scientists and Specialists including Health" (SOC 192041, hourly wage rate of $41.83), "Biological Scientists" (SOC 191020, hourly wage rate of $37.44), "Animal Scientists" (SOC 191011, hourly wage rate of $34.46). The average wage rate among these occupations is $39.90. Clerical assistance is valued using SOC 434071 ("File Clerks") reported at $14.42 per hour. Before calculating the estimated labor cost we multiply the reported wage rate by 2—a commonly used multiplier—to adjust the median hourly wage rate for benefits and overhead.

Estimated total cost for each of the additional proposed responsibilities is determined by multiplying the number of entities affected by the annual reporting frequency per entity affected and the unit labor cost (see Table 6B). Unit cost of labor for each reporting responsibility is calculated as the labor hours per entity involved in the specific reporting task times the wage rate. For instance, total cost of $0.57 million for reporting responsibility code R01 ("Provide test, control, and reference article characterization and risk information") is calculated as follows: 1,316 respondents x 5 average annual responses per respondent x (0.75 hours x $105.60 per hour + 0.25 hours x $28.84 per hour). The reporting costs for the remaining reporting responsibilities, R02-R12, are calculated in a similar fashion. Adding the estimated costs across all entities affected provides an estimated annual cost of the proposed rule of $5.8 million. We note that even though Table 6B provides costs disaggregated by entity responsible; these costs will be mainly paid by the sponsor funding the nonclinical laboratory study.

Table 6B.--Estimated Reporting Costs of the Proposed Rule

Main Entity Responsible[1]	Additional Reporting Responsibility	Number of Entities Affected	Average Annual Reporting	Labor Hours (per response)			Unit Cost	Total Cost (millions)
				Total Hours per Response	Main Entity	Clerical Assistant		
Sponsor	R01	1316	5	1	0.75	0.25	$86.41	$0.57
	R02	10	1	15	11.25	3.75	$1,296.15	$0.01
Quality Assurance Unit (QAU)	R03	300	60.25	0.25	0.19	0.06	$21.60	$0.39
Management with Executive Responsibility	R04	10	2	5	3.75	1.25	$432.05	$0.01
	R05	300	10	0.5	0.38	0.13	$43.21	$0.13
Study Director	R06	300	60.25	2	1.50	0.50	$172.82	$3.12
	R07	300	60.25	0.5	0.38	0.13	$43.21	$0.78
	R08	300	2	2	1.50	0.50	$172.82	$0.10
Independent Contributing Scientist or Principal Investigator	R09	30	1	5	3.75	1.25	$335.28	$0.01
	R10	200	10	1	0.75	0.25	$67.06	$0.13
	R11	200	5	8	6.00	2.00	$536.45	$0.54
Total								$5.8

[1] Hourly median wage rate for sponsor, QAU, and management with executive responsibility is $105.60, $79.80 for contributing scientists or principal investigators, and $28.84 for clerical assistants. Total may not add up due to rounding. See Table 6A for a description of each reporting code. The number of affected entities and additional burden come from the Paperwork Reduction Act estimates in the preamble.

Recordkeeping Costs

The proposed rule proposes additional recordkeeping responsibilities from multiple entities involved in the conduct of a nonclinical laboratory study to enhance the information that is essential for appropriate conduct of nonclinical laboratory studies, e.g., documenting protocol and SOPs approval, documenting training and inspectional findings. Table 6C below briefly describes the additional proposed recordkeeping requirements, and the proposed entity responsible for ensuring each of the additional requirements is fulfilled.

Table 6C.--Additional Recordkeeping Responsibilities Proposed by Rule

Main Entity Responsible[1]	Additional Documentation Responsibility
Sponsor	K01. Protocol approval, including all amendments
	K02. Animal welfare determination
	K03. Accreditation status of person conducting the animal testing
	K04. Test, control, and reference article parameters
	K05. Archival locations
	K06. Qualifications of contracted persons

Management with executive responsibility	K07. Training and experience on GLP
	K08. Training and experience on animal care
	K09. All persons are qualified for multisite studies
	K10. Periodic review of GLP Quality System
	K11. Periodic review of QAU
	K12. Appointment of management representative
	K13. All test sites have master schedule
	K14. Appointment of person to manage master schedule
	K15. Selection of lead QAU for multisite studies

Quality Assurance Unit (QAU)	K16. Process-based inspections
	K17. Audits of final reports of contributing scientists
	K18. Audits of principal investigator reports
	K19. Audits of final study reports for multisite studies
	K20. Review of protocols and amendments
	K21. Review of SOPs and amendments as they pertain to specific studies
Study Director	K22. Multisite need for PIs
	K23. Document communications
	K24. Compliance with protocol
	K25. QAU review of protocol and applicable SOPs
	K26. Management provided adequate resources
	K27. Computerized systems validated
	K28. Review by animal study review board
	K29. Multisite personnel qualified
	K30. Test system as required
	K31. GLP compliance
	K32. Test article accountability when containers disposed of
Independent Contributing Scientist	K33. Education, training, and experience
	K34. Archive location
	K35. Appropriate animal care (when applicable)
Principal Investigator	K36. Protocol and protocol amendment acceptance
	K37. Study deviations
	K38. Archive location

[1] Task may involve other assistance such as clerical.

To estimate recordkeeping costs we use the same wage rates discussed in section E1 above. However, we assume that documentation and recordkeeping activities involve 75 percent of the total labor hours allocated to clerical assistants and 25 percent to the main entity responsible for the documentation. Thus, after adjusting for benefits and overhead, the hourly wage rate for

entities with a managerial role ("Management Occupations," SOC 110000) is $105.60 and $28.84 for clerks ("File Clerks," SOC 434071).

Estimated total cost for each of the additional recordkeeping responsibilities is determined by multiplying the number of entities affected by the annual recordkeeping frequency per entity affected and the unit labor cost (for brevity we provide this information in Table A1 of the Appendix to the PRIA). Unit cost of labor for each recordkeeping responsibility is calculated as the labor hours per entity involved in the specific task times the wage rate. For instance, total cost of $10.53 million for responsibility K01, "Protocol approval, including all amendments", is calculated as follows: 2,193 respondents x 100 responses per respondent x (0.25 hours x $105.60 per hour + 0.75 hours x $28.84 per hour). The recordkeeping costs for the remaining responsibilities, K02-K38, are calculated following the same approach.

Table 6D below provides a summary of the recordkeeping costs by the main entity responsible. Total estimated annual cost is $27.6 million. Again, even though the proposed recordkeeping responsibilities would be required from entities other than the sponsor, all costs are assumed to be ultimately borne by the sponsor funding the nonclinical laboratory study.

Table 6D.--Estimated Annual Recordkeeping Cost

Main Entity Responsible	Cost Item Codes	Estimated Cost ($million)
Sponsor	K01-K06	$13.75
Management with executive responsibility	K07-K15	$1.93
Quality Assurance Unit (QAU)	K16-K21	$6.36
Study Director	K22-K32	$5.41
Independent Contributing Scientist	K33-K35	$0.00
Principal Investigator	K36-K38	$0.14
Total		$27.60

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

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

14. Annualized Cost to the Federal Government

We estimate no cost to the Federal government as the information collection is supported by existing resource allocations.

15. Explanation for Program Changes or Adjustments

The information collection is being revised through agency rulemaking. We believe the one-time reporting and recordkeeping burdens introduced by the proposed regulations (cumulatively estimated to be 9,693 responses and 128,590 hours) will be realized upon their implementation, if finalized. Also, if the proposal is finalized, *existing* burden for the information collection as currently approved (now 36,150 responses and 1,304,157 hours) will be absorbed into the recurring burden we have estimated for the proposed regulations.

16. Plans for Tabulation and Publication and Project Time Schedule

The reporting requirements contained in this proposal are not statistical in nature and the records are not published for statistical use.

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

Display of OMB Expiration Date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.