Attachment H – Consultation Responses

AMERICAN CHEMISTRY COUNCIL

Antimicrobial Exposure Assessment Task Force II

2015/2016 Consultation for ICR Renewal for Submission of Protocols and Study Reports for Environmental Research Involving Human Subjects Identified by EPA ICR No. 2195.05 and OMB Control No. 2070–0169

March 9, 2016

In response to the U.S. Environmental Protection Agency's request for external consultation on the renewal of the Information Collection Request (ICR) for the federal human research regulations[1] the American Chemistry Council's Antimicrobial Exposure Assessment Task Force II (AEATF II) provides the following information.

1. Publicly Available Data

a. Are the data that the Agency seeks available from any public source, or already collected by another office at EPA or by another agency?

In some cases, publically available data exist. Any existing public data are reviewed by AEATF II to determine if they meet the technical needs and the current quality standards prior to generation of new data.

b. If yes, where can you find the data? Is the available data truly duplicative, or are only certain data elements available which may not address our data requirements very well?

Publically available data can be found in the published literature and publically available databases. Typically, the available data are not truly duplicative as many critical elements are missing, they are not representative of the scenario being investigated or they are lacking quality control aspects. Another potential issue is that any data generated with human volunteers must meet current ethics standards; sometimes the information needed to determine whether those standards are met is missing or unavailable in which case the data cannot be used.

2. Frequency of Collection

a. Can the Agency collect the information less frequently and still produce the same outcome?

[1] ***See* 80 Fed. Reg. 80360 (Dec. 24, 2015).**

The AEATF II does not believe that Agency is seeking the human exposure data too frequently.

3. Clarity of Instructions

a. The rule is intended to require respondents to provide certain data for the Agency's use. Is it clear from the regulations and other Agency guidance what you are required to submit and how to submit it? If not, what suggestions do you have to clarify the information?

The rule gives a general explanation of the process, but does not specify what needs to be submitted, how it needs to be submitted, and the steps leading up to the submission. In addition, the required changes to human subject recruitment and consenting processes since 2006 are not clearly documented. These new procedures and requirements need to be incorporated into a revision to the OCSPP Series 875 Test Guidelines.

b. Do you understand that you are required to maintain records?

Yes, keeping detailed records is standard practice for the AEATF II as part of Good Laboratory Practice regulations. However, the volume of records that are generated and that must be retained has increased significantly. The number of pages in study protocols and final reports has increased 10 to 15 fold as a result of the EPA's 2006 rule, Protections for Subjects in Human Research (2006 Rule).

c. Is it difficult to format the information for submission so that it is clear, logical and easy to understand?

The issue with formatting the submission is that it is very time-consuming due to the large number of documents required for each study submission, including multiple versions of the documents (e.g., protocol, informed consent form, survey reports, detailed sampling plans, SOPs, IRB correspondence, IRB review reports, recruitment flyers, researcher CVs, Spanish translations, etc.). Prior to the 2006 Rule, protocol submissions consisted of about 40 pages. After the 2006 Rule became effective, that submission increased to over 500 pages, which are arranged in volumes to make the review of the submission more manageable. Just the process of arranging and checking the final documents for a protocol submission involves a minimum of two people, one technical and one clerical, for approximately two to four days.

d. Are there forms associated with this process? If so, do you use them? Are they clear, logical, and easy to complete?

The only form provided by EPA is a short checklist of items specified under 40 CFR 26.1125 that must be included in each protocol submission. The form is d e r i v e d from the regulation, and is not particularly detailed or time-consuming to complete once all of the documents have been formatted and paginated into the submission volumes. There is some duplication of information

*requested on the form. This form has not been updated since it appeared in 2006, and t**he form could be improved as it does not ask for sufficient detail to clearly capture all of the key information that a reviewer might need especially if the protocol has been reviewed by the IRB multiple times.***

4. Electronic Reporting and Record Keeping

The Government Paperwork Elimination Act requires that agencies make available electronic reporting alternatives to paper-based submissions. Entities that submit study protocols and/or reports in response to EPA's 2006 final rule may elect to submit the information either on paper, or electronically, via email, CD, or DVD.

a. What do you think of electronic alternatives to hard-copy data submissions?

The AEATF II is almost paperless in its documentations, so it prefers electronic submissions.

b. Are you keeping your records electronically? If yes, in what format?

Yes, AEATF II records are kept in several forms including MS Word, Excel, Adobe Acrobat, JPEG, and e-mail files. The only hard copy documents handled by AEATF II are study raw data that are archived and hard copy reports that are still being required for submissions to EPA.

c. Does electronic submission benefit you by reducing your burden or permitting greater efficiency in compiling the information?

Since all documents associated with the protocol or study report are generated and stored electronically, an electronic submission is easier. The AEATF II submits final reports "electronically", although three hard copies are also required for submission to the EPA Document Processing Desk. These final report documents can be over 1,000 pages making this a time-consuming and environmentally wasteful requirement. ***Electronic submissions could be even more beneficial if the need for paper hard copies was entirely eliminated. Other EPA departments, including the Antimicrobials Division (AD), no longer require paper documents; the AEATF strongly urges the EPA Document Processing Desk to adopt a policy for electronic submissions.***

5. Burden and Costs

a. The labor rates EPA will use to estimate costs for regulated entities are taken from the May 2014 National Industry-Specific Occupational Employment and Wage Estimates for NAICS code 541710 (Research and Development in the Physical, Engineering, and Life Sciences), published by the Bureau of Labor Statistics. The BLS fully-loaded hourly rates for this industry are $168/hour for management, $87/hour for technical staff, and $50/hour for clerical staff. Do you think these labor rates are appropriate? Can you suggest another NAICS code that would be more appropriate?

The labor rates used by EPA are lower than that incurred by the AEATF II, especially for the technical staff. The professional technical and management work of the AEATF II is done by highly specialized research scientists with MS or PhD degrees who work for the AEATF II on a consulting basis. The more appropriate rates are $260, $200, and $60 per hour for the management, technical, and clerical classifications, respectively.

b. EPA will estimate annual costs by multiplying the estimated average cost of burden hours associated with each of several classes of activities by the estimated number of times each year that class of activity is expected to be performed.

Please enter in Table 1 on the next page your estimates of the incremental paperwork burden in hours by management, technical, and clerical staff associated with each occurrence of each activity listed. Base your estimates on your experience since the rule became effective in 2006, and on your projections for the paperwork and recordkeeping burden of each activity over the period covered by the ICR renewal—i.e., between September 1, 2016 and August 31, 2019.

Please explain how you arrived at your estimates, and please estimate only the incremental burden imposed by the paperwork requirements associated with the rule, not the costs of conducting the research or costs you would have incurred if the rule were not in effect.

Table 1
Respondent Burden Estimates:
Unit Costs of Discrete Activities Required by the New Rule

Activities	Average Burden Hours Per Occurrence			Total Per Response		
	Manage-ment $168[1]	Technical $87	Clerical $50	Total Hours	Cost ($) Based on EPA Nos.	Based on Industry[1] Cost ($)
Rule familiarization and training (per protocol)[2]	8	10	7	25	$2,564	$4,500
Prepare and submit protocol for IRB review[3]	25	225	30	280	$25,275	$53,300
Prepare and submit protocol for EPA and HSRB review[4]	100	500	40	640	$62,300	$128,400

Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol[5]	20	150	20	190	$17,410	$36,400
*Prepare and submit final report for EPA and HSRB review**	40	800	40	880	$78,320	$172,800
Store, file, and maintain records[6]	10	40	10	60	$5,660	$11,200
TOTALS	203	1,765	147	2,075	$191,529	$406,600

**Note this is an activity that AEATF spends significant time on since the 2006 rule, which was missing from this table, but which we feel needs to be included.*

Notes for Table 1:

1 Rates are from the May 2014 National Industry-Specific Occupational Employment and Wage Estimates for NAICS code 541710 (Research and Development in the Physical, Engineering, and Life Sciences), published by the Bureau of Labor Statistics.

A column was added that reflects more representative estimated costs to the AEATF II based on typical industry labor costs ($260, $200, and $60 per hour for the management, technical, and clerical classifications, respectively)

2 Consider this a one-time activity. Enter your estimate of what your total burden will be for rule familiarization and training during 2016-2019. Since you are already familiar with the rule, you may have little additional burden for this activity.

This is not entirely a one-time activity due to new people coming on board, normal turn-over of personnel, and training present personnel on changes in the process as they occur. In addition, requirements change from study to study as HSRB reviews of previous studies can impose new requirements, particularly for documentation and/or justification of various protocol aspects. In the latter situation, some level of re-training for each new study or report generated is required.

3 Estimate your average paperwork burden of preparing for a single IRB review which would not have occurred but for the requirements of the human studies rule. Consider IRB reviews both before and after EPA/HSRB review.

4 Estimate your average paperwork burden of preparing a single submission to EPA of a protocol proposing research involving intentional exposure of human subjects. Treat each repellent testing protocol as a single protocol, however many test materials may be involved.

The amount of background research required for designing and documenting the studies as currently required by the Agency and the HSRB has markedly increased. This is in addition to the extra work now required to prepare the final

submission package for EPA/HSRB review. For this task "management" includes not only the task force manager, but other sponsor company members (registrants) who make up the protocol committee and are directly involved with the protocol development and oversight.

5 Estimate your average paperwork burden to document the ethical conduct of a single study for submission to EPA when the protocol has already been reviewed by EPA and the HSRB. Treat all reports reflecting a single execution of one protocol as a single activity, however many test materials may be involved.

6 Estimate your average paperwork burden for managing and archiving records of each submitted protocol or study report.

There is additional work now associated with managing, storing and archiving documents as records containing confidential subject information (ICF, comprehension forms, subject information forms) are to be kept separate from the raw data files.

c. Please estimate in Table 2 below the frequency with which you expect to incur the paperwork burden associated with each class of activity described in Table 1. Your responses will be combined with those from others in EPA's revised burden estimate. Please explain any assumptions underlying your estimates.

The AEATF II is approaching the last few years of its research program, so the paperwork burden will subside significantly by late 2018 because it will no longer be submitting protocols or final reports.

Table 2
Respondent Burden Estimates: Estimated Frequency of Activities

Activities	Projected Number of Occurrences by Year		
	Sept 2016-Aug 2017	Sept 2017-Aug 2018	Sept 2018-Aug 2019
Prepare and submit protocol for IRB review[1]	4	0	0
Prepare and submit protocol for EPA and HSRB review[2]	4	0	0
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol[3]	3	1	0
*Prepare and submit final report for EPA and HSRB review**	3	1	0
Store, file, and maintain records	3	1	0

**Note this is an activity that AEATF spends significant time on since the 2006 Rule, which was missing from this table, but which we feel needs to be included.*

Notes for Table 2:

[1] Count IRB submissions that would not have occurred but for the requirements of the human studies rule, including those both before and after EPA/HSRB review.

[2] Count each repellent testing protocol as a single occurrence, however many test materials it may involve.

[3] Count each executed repellent protocol only once, however many test materials or physical study volumes it may involve.

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d. The Agency assumes there are no capital costs within the scope of this Information Collection Request. Do you agree?

The AEATF II agrees.

e. Are there other activities or incremental costs associated with the paperwork burden imposed by the human studies rule, not listed in the tables but which should be accounted for?

New SOPs and revisions to SOPs have been required to address the changes imposed by the human studies rule. Although a number of new and updated SOPs now exist, continual revisions are still needed based on feedback from EPA and the HSRB. There are management, technical, and clerical costs associated with this activity.

2015/2016 Consultation for OPP ICR Submission of Protocols and Study Reports for Environmental Research Involving Human Subjects

Response by Agricultural Handler Exposure Task Force (AHETF)

DRAFT

1. Publicly Available Data

a. Are the data that the Agency seeks available from any public source, or already collected by another office at EPA or by another agency?

No. Existing public data and existing data submitted to regulatory agencies in the U.S. and other countries by AHETF members were reviewed by AHETF for applicability to its needs prior to the generation of new data.

b. If yes, where can you find the data? Is the available data truly duplicative, or are only certain data elements available which may not address our data requirements very well?

This is not applicable to the AHETF.

2. Frequency of Collection

a. Can the Agency collect the information less frequently and still produce the same outcome?

This is not applicable to the AHETF.

3. Clarity of Instructions

a. The rule is intended to require respondents to provide certain data for the Agency's use. Is it clear from the regulations and other Agency guidance what you are required to submit and how to submit it? If not, what suggestions do you have to clarify the information?

The rule gives a general overall explanation of the process but does not cover exactly what and how it needs to be submitted. However, after considerable interaction with EPA since 2006, the AHETF now knows what and how to submit data successfully. However, other registrants who have not had this interaction will likely have difficulty knowing how to make submission. EPA should consider developing guidelines.

b. Do you understand that you are required to maintain records?

Yes, keeping detailed records is standard practice for the AHETF as part of the Good Laboratory Practice (GLP) regulations. However, the volume of records that need to be kept has increased significantly. The number of pages in protocols and final reports has increased 10 to 15 fold as a result of the final rule.

c. Is it difficult to format the information for submission so that it is clear, logical and easy to understand?

The format is now clear and standardized but it is still time-consuming for the AHETF to format the submission materials due to the large number of documents required for each study (e.g., protocol, informed consent form, survey reports, detailed sampling plans, SOPs, IRB correspondence, flyers, letters to qualified study participants, Spanish translations, etc.). Prior to the final rule, protocols contained about 40 pages. After the final rule became effective, that number increased to over 2000 pages. The AHETF and EPA then agreed to some efficiency that lowered the number of pages to 400 to 550 (still more than 10 times what it was before the final rule).

d. Are there forms associated with this process? If so, do you use them? Are they clear, logical, and easy to complete?

The institutional review board (IRB) has several forms that need to be completed. The only form provided by EPA is a checklist of items from the rule that must be covered in every protocol. The form is taken directly from the rule and is not especially difficult to complete, but does take a significant amount of time. In order to improve the clarity and efficiency of the protocol and report submissions, AHETF created new formats and tables to convey the information required.

4. Electronic Reporting and Record Keeping

The Government Paperwork Elimination Act requires that agencies make available electronic reporting alternatives to paper-based submissions. Entities that submit study protocols and/or reports in response to EPA's 2006 final rule may elect to submit the information either on paper, or electronically, via email, CD, or DVD.

a. What do you think of electronic alternatives to hard-copy data submissions?

The AHETF is almost paperless in its documentations, so it definitely prefers electronic submissions.

b. Are you keeping your records electronically? If yes, in what format?

Yes, records are kept in several forms including MS Word, Excel, Adobe Acrobat, E-mail files, and CDs. Key documents are also stored on a task force server for easy access by AHETF members and EPA. The only hard copy documents handled by AHETF are study raw data that are archived and hard copy reports that are required for submissions to EPA.

c. Does electronic submission benefit you by reducing your burden or permitting greater efficiency in compiling the information?

Most of the information is generated electronically, so converting this to hard copy for the submission is an additional burden. The AHETF submits final

*reports "electronically", although two hard copies of each report are submitted prior to the electronic sending. It is with the hard copy submission that the MRID number is assigned. Reducing the effort to **only** the electronic submission (and somehow obtaining the necessary MRID number prior to this) would be helpful to the efficiency of the overall submission process.*

5. Burden and Costs

a. The labor rates EPA will use to estimate costs for regulated entities are taken from the May 2014 National Industry-Specific Occupational Employment and Wage Estimates for NAICS code 541710 (Research and Development in the Physical, Engineering, and Life Sciences), published by the Bureau of Labor Statistics. The BLS fully-loaded hourly rates for this industry are $168/hour for management, $87/hour for technical staff, and $50/hour for clerical staff. Do you think these labor rates are appropriate? Can you suggest another NAICS code that would be more appropriate?

The rates used by EPA are less than that incurred by the AHETF, especially for the technical people. The professional technical and management work of the AHETF is done by highly specialized research scientists who work for the AHETF on a consulting basis, so a classification for researchers with MS or Ph.D. degree requirements would be more appropriate. The more applicable rates for the next three years are $250, $200, and $60 per hour for the management, technical, and clerical classifications, respectively. This does not account for the sweat equity that goes into these programs by representatives of the member companies whose time is not charged to the AHETF.

b. EPA will estimate annual costs by multiplying the estimated average cost of burden hours associated with each of several classes of activities by the estimated number of times each year that class of activity is expected to be performed.

Please enter in Table 1 on the next page your estimates of the incremental paperwork burden in hours by management, technical, and clerical staff associated with each occurrence of each activity listed. Base your estimates on your experience since the rule became effective in 2006, and on your projections for the paperwork and recordkeeping burden of each activity over the period covered by the ICR renewal—i.e., between September 1, 2016 and August 31, 2019.

Please explain how you arrived at your estimates, and please estimate only the incremental burden imposed by the paperwork requirements associated with the rule, not the costs of conducting the research or costs you would have incurred if the rule were not in effect.

The estimates are based on AHETF records on hours spent by consultants and actual costs.

Table 1
Respondent Burden Estimates:
Unit Costs of Discrete Activities Required by the New Rule

Activities	Average Burden Hours Per Occurrence			Total Per Response		
	Mgt $168[1]	Technical $87	Clerical $50	Total Hour	Cost ($) Estimated by EPA	Actual Cost ($) to AHETF
Rule familiarization and training (per protocol)[2]	*0*	*0*	*0*	*0*	*0*	*0*
Prepare and submit protocol for IRB review[3]	*0*	*0*	*0*	*0*	*0*	*0*
Prepare and submit protocol for EPA and HSRB review[4]	*0*	*0*	*0*	*0*	*0*	*0*
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol[5]	*65*	*2000*	*60*	*2125*	187,920	419,850
Store, file, and maintain records[6]	*5*	*5*	*5*	*15*	1,525	2,550
TOTALS	70	*2005*	*65*	2,140	489,445	422,400

Notes for Table 1:

[1] Rates are from the May 2014 National Industry-Specific Occupational Employment and Wage Estimates for NAICS code 541710 (Research and Development in the Physical, Engineering, and Life Sciences), published by the Bureau of Labor Statistics.

Please note: In case you wish toad it, a column was added that reflects the actual costs to the AHETF.

As stated above, the AHETF uses highly qualified technical consultants for doing the research, including preparation of protocols and reports. Their rates are higher than those specified by the Department of Labor.

[2] Consider this a one-time activity. Enter your estimate of what your total burden will be for rule familiarization and training during 2016-2019. Since you are already familiar with the rule, you may have little additional burden for this activity.

[3] Estimate your average paperwork burden of preparing for a single IRB review which would not have occurred but for the requirements of the human studies rule. Consider IRB reviews both before and after EPA/HSRB review.

This is not applicable to the AHETF since it will not be submitting any protocols in 2016-2019

[4] Estimate your average paperwork burden of preparing a single submission to EPA of a protocol proposing research involving intentional exposure of human subjects. Treat each repellent testing protocol as a single protocol, however many test materials may be involved.

This is not applicable to the AHETF since it will not be submitting any protocols in 2016-2019

[5] Estimate your average paperwork burden to document the ethical conduct of a single study for submission to EPA when the protocol has already been reviewed by EPA and the HSRB. Treat all reports reflecting a single execution of one protocol as a single activity, however many test materials may be involved.

This cost is increasing significantly and continually due to difficulties in recruiting study participants under the ethics rules established by the Agency and the HSRB. . The recruitment process requires very extensive documentation and record keeping by those who assemble lists of names, direct initial phone calls, make more detailed follow up phone calls, and visit with potential cooperators at their locations.

[6] Estimate your average paperwork burden for managing and archiving records of each submitted protocol or study report.

c. Please estimate in Table 2 below the frequency with which you expect to incur the paperwork burden associated with each class of activity described in Table 1. Your responses will be combined with those from others in EPA's revised burden estimate. Please explain any assumptions underlying your estimates.

The AHETF is approaching the end of its research program, so the paperwork burden will subside significantly only because it will no longer submit protocols and only has a few more reports to complete.

Table 2
Respondent Burden Estimates: Estimated Frequency of Activities

Activities	Projected Number of Occurrences by Year		
	Sept 2016-Aug 2017	**Sept 2017-Aug 2018**	**Sept 2018-Aug 2019**
Prepare and submit protocol for IRB review[1]	*0*	*0*	*0*
Prepare and submit protocol for EPA and HSRB review[2]	*0*	*0*	*0*
Document ethical conduct of a completed study for which EPA and the HSRB have reviewed the protocol[3]	*2*	*2*	*0*
Store, file, and maintain records	*12*	*12*	*0*

Notes for Table 2:

[1] Count IRB submissions that would not have occurred but for the requirements of the human studies rule, including those both before and after EPA/HSRB review.

[2] Count each repellent testing protocol as a single occurrence, however many test materials it may involve.

[3] Count each executed repellent protocol only once, however many test materials or physical study volumes it may involve.

d. The Agency assumes there are no capital costs within the scope of this Information Collection Request. Do you agree?

The AHETF agrees.

e. Are there other activities or incremental costs associated with the paperwork burden imposed by the human studies rule, not listed in the tables but which should be accounted for?

The AHETF is not immediately aware of applicable activities.