AMERICAN CHEMISTRY COUNCIL
Antimicrobial Exposure Assessment Task Force II

DATA REVIEW AND STUDY ACCEPTANCE CRITERIA

For Inclusion of Existing Antimicrobial Exposure Monitoring Studies In The Antimicrobial Exposure Assessment Task Force II (AEATF II) Database

November 28, 2006

I. DATA REVIEW PROCESS

All existing antimicrobial exposure monitoring studies, when offered by a third party for sale, will undergo a 3-step review process to determine whether they meet the selection criteria listed in this document. In addition to the specific review process outlined below, a continued dialogue will take place with U.S. EPA, the Canadian Pest Management Regulatory Agency (PMRA) and the California Department of Pesticide Regulation (CDPR) to discuss each exposure scenario to be studied and the general study design elements (e.g., worker tasks, equipment, locations, replicates) proposed by AEATF II. This discussion will serve to inform the existing study review team as to the minimum study design and data collection requirements needed for an existing study to be deemed acceptable to at least partially fulfill a given data requirement. The non-acceptance of a given study, via the AEATF II study review process, does not imply that it is not suitable for use by any individual member company to fulfill a specific data requirement, only that the AEATF II has made the determination that the study will not be purchased for broader use by the AEATF II member companies.

A. <u>Preliminary Review</u>

1. The preliminary review will be conducted by the study submitter (or a designated representative) and provided to AEATF II along with a complete copy of the study report at the time the study is submitted to the Task Force for consideration.
2. The AEATF II will consider all studies, including any that are presently in PHED version 1.1 or version 2. The studies in PHED version 1.1 are all more than 15 years old and are not subject to data compensation requirements. However, these data were originally submitted to PHED without attribution to compound or company ownership. If any of these data fulfill acceptance criteria, they could potentially provide very beneficial information that would complement data developed by AEATF II.
3. Raw data for a study must be made available, if requested.
4. A list of potential studies and all preliminary review forms and reports should be submitted by dates requested by AEATF II.
5. The purpose of the preliminary review will be to eliminate the submission of studies that clearly do not meet the selection criteria, and to serve as a check on

the availability and submission of supporting information.

6. AEATF II will provide an Excel spreadsheet to the submitter for use in summarizing the study details and data.
7. AEATF II will provide a confidentiality agreement to the submitter to protect the proprietary nature of the data and the study.

B. Intermediate Review

1. The intermediate review will be conducted by a qualified AEATF II contractor, hired and trained for this purpose.
2. The purpose of the intermediate review will be to verify the accuracy of the preliminary review and, where necessary, provide a more detailed discussion summarizing each specific area of the criteria, including whether each criterion was met and possible deficiencies in the study data.
3. The intermediate review will be evaluated and a determination made as to whether the study or any of the data could be used in the AEATF II database. Only studies that have met the design considerations will be presented to EPA, PMRA and CDPR for final review.

C. Final Review

1. A Committee consisting of representatives from the AEATF II and EPA, PMRA and CDPR will make the final review and decision on whether a study is accepted for purchase.
2. The intermediate review by the contractor of studies will be made available to the Committee and will serve as the basis for the final review.
3. Studies or portions of studies selected after final review will then be considered for purchase by the AEATF II for inclusion in the Task Force database.
4. Reports for studies that the Committee deems not acceptable for the AEATF II database will be returned to the submitter with an explanation as to why the study did not meet the selection criteria. Reports of studies that are purchased by AEATF II will be placed in the AEATF II archives.

D. Appeals Process

Study contributors whose studies are not accepted for possible purchase may appeal that decision, but should do so within 30 days of such notification.

II. STUDY ACCEPTANCE CRITERIA: STUDY DESIGN CONSIDERATIONS

- All monitored activities and equipment must be described in detail and representative of typical antimicrobial handling practices.
- It should be clear that the individuals monitored 1) either are normally employed in the mixing/loading and/or application of antimicrobial products or pesticide products

and handled them comparably, or, 2) if consumers (i.e., non-professionals), are applying antimicrobials products by methods they would use in the course of their normal activities. .

- Appropriate supporting information such as the formulation type, mixing and application method, application rate, duration of the work cycle, amount of AI handled/replicate, etc. must be available.
- The use of protective equipment (PPE) is acceptable but must be part of normal work practices.
- The study location and environmental/weather conditions during the monitoring period should be available.
- All elements of a given study may not have been conducted under GLP, but must have critical elements of GLP e.g., protocol, final report, and raw data available in order to be considered by the AEATF II.

III. STUDY ACCEPTANCE CRITERIA: EXPOSURE MONITORING

A. Field Aspects

1. Field recoveries should have been collected on a site-specific basis for time periods and environmental conditions representative of those during collection of field activity exposure samples.
2. Field fortification data should include at least triplicate samples at two rates and triplicate samples of controls; however, duplicate samples will be considered with justification.
3. Dermal exposure monitoring techniques should be specified and should include one of the following approaches. Note that glove washes of chemical resistant gloves are not an allowable method.

    a. whole-body dosimeters inside and/or outside of typical clothing plus hand (cotton gloves can substitute for hand exposure) and head/face exposure determinations,
    b. a minimum of 10 patch dosimeters attached inside or outside normal work clothing to the chest, back, both upper arms, both lower arms, both upper legs, both lower legs, plus hand (cotton gloves can substitute for hand wash) and head/face exposure determinations (exceptions for head/face and upper arms and upper or lower legs and bilateral measurements will be considered on a case by case basis). Conversion and use criteria have been developed by the NAFTA harmonization group and should be considered for adaptation of the PHED data.
    c. Combination of patches and clothing that are representative of the whole body, including hand and head/face exposure determinations.

4. Inhalation exposure – Inhalation data are required if the vapor pressure of the chemical under study is $>10^{-4}$ mm Hg or if the chemical is used in an environment that results in significant volatilization (e.g., around steam pipes or

in metal working fluids), or if the method produces inspirable aerosols. If data were collected, inhalation exposure should have been measured by sampling the person's breathing zone.

5. Exposure monitoring duration – The monitoring period should be at least half of a normal work period duration or mix/load and/or apply at least half of the daily amount normally used.
6. If the exposure monitoring duration does not meet the requirement of item number 5, then the number of non-detects/less than LOQ values should account for less than 40% for dermal exposure. This cut-off is specified because the distribution of exposures can be reasonably extrapolated from a data set with up to 40% non-detects. Data sets with ≥50% non-detects produce a degree of uncertainty deemed unacceptable for a generic database.
7. If the exposure monitoring duration and number of non-detects/less than LOQ values do not meet the criteria in items 5 and 6, then the LOQ should be no more than 20 ng/cm^2 for average dermal exposure (across body part areas) and no more than 500 ppb for hand wash solution. The LOQ cutoffs are conservative in that if all data were at the LOQ, the resulting calculated exposure (at ½ LOQ) would yield an MOE of ≥100 for a compound with a systemic (absorbed dose) NOAEL ≥1 mg/kg.

♦ B. Analytical Aspects - QA/QC

1. Analytical methods should have been validated for each analyte and substrate by the performing laboratory including establishment of the method's working concentration range to cover values anticipated in the field studies, determination of detector response over a reasonable standard concentration range, and determination of the accuracy and precision of the method within the analytical environment.
2. The study should include both field fortification samples and concurrent laboratory spikes.
3. The average recoveries of lab spikes should be between 70-120 percent and the precision value (coefficient of variation; CV) should be less than or equal to 20 percent.
4. Recovery of field fortification samples should be 50-120% with a C.V. ≤25%.
5. Exposure samples should have been analyzed in such a manner that the stability of each analyte in each substrate was assessed for the entire time period from collection to analysis.

♦ C. Biomonitoring

Biological monitoring studies will be accepted for further review if they meet the selection criteria (excluding passive dosimetry) and there is a primate (human or monkey) dermal absorption study for the chemical monitored and pharmacokinetic data identifying the major excretory metabolite or parent compound.