REREGISTRATION

ENVIRONMENTAL RISK SCIENCE CHAPTER FOR CACODYLIC ACID AND ITS SODIUM SALT

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ENVIRONMENTAL RISK SCIENCE CHAPTER
CACODYLIC ACID AND ITS SODIUM SALT
$[(CH_3)_2AsO(OH)/(CH_3)_2AsOO^-Na^+]$

USE CHARACTERIZATION

Cacodylic acid and its sodium salt are nonselective contact herbicides that defoliate or desiccate a wide variety of plant species. Most registered products contain a mixture of the acid and salt. The primary use of cacodylic acid/Na salt is as a cotton defoliant. A small proportion of the use is for noncrop sites, including utilities, residential outdoor, and weed treatment around the bases of citrus trees. Current labels for irrigated and dryland cotton allow application of up to 1.2 lb ai/A annually by either aerial or ground spray. However, the registrant has proposed reducing the maximum application rate on cotton to 0.6 lb ai/acre; therefore, this rate also will be included in the assessment. Treatment on cotton is made when 50% or more of the bolls have opened (7 to 10 days prior to the anticipated picking date).

Application rates for noncrop sites are mostly higher than for cotton; however, for many products, directions simply specify mixing a certain amount of product in a specified number of gallons of water and applying the spray solution to the point of runoff. Application for noncrop sites is by ground only. Because cacodylic acid/Na salt produces a top-kill only, repeat applications are needed for season long weed control. Some labels limit the number of applications to three per year but many simply state that repeat applications can be made as needed.

The following application information, obtained from product labels and the registrant's proposed reduction in the application rate for cotton, is used for assessing ecological risk:

Application Information

Site	Max. Appl. Rate (lb ai/A)	Max. No. Appl.	Appl. Interval	Appl. Method
Cotton	0.6 - 1.2 [1]	1	n/a	ground or aerial spray
Noncrop areas	2.5 - 8.1 [2]	3 [3]	not specified	ground spray
Orchard (understory)	0.2 - 5.0 [2]	3 [3]	not specified	ground spray

[1] the maximum labeled rate is 1.2 lb ai/A; however, the registrant has proposed a maximum of 0.6 lb ai/A

[2] the maximum application rate is higher on some labels than on others

[3] some labels limit the number of applications, others indicate to reapply as needed; 3 applications were selected to cover a reasonable likelihood of repeat applications

For terrestrial risk, in addition to the 3 applications for noncrop and orchard understory, the Agency also is calculating exposure and potential risk from a single application at 5 lb ai/acre (orchard understory) and 8.1 lb ai/acre (noncrop areas).

RISK CONCLUSIONS AND RISK CHARACTERIZATION (see Appendix 1 for definitions and explanations of terms and acronyms)

Based on a screening assessment, the Agency concludes that small mammals and terrestrial plants are at risk from exposure to cacodylic acid/Na salt at registered use sites. The greatest risk occurs from applications at noncrop sites, especially for the highest use rates. Cotton has the lowest maximum application rate (1.2 lb ai/A), and the registrant has proposed to reduce it to 0.6 lb ai/A. The Agency's risk conclusions for plants and animals are summarized below.

Mammals: Concern exists for small mammals exposed to cacodylic acid/Na salt. Whereas all application rates at all use sites represent a potential for risk, the risk from noncrop use and the high rate in orchards is substantially greater than risk from the cotton use at 1.2 lb ai/acre. The proposed reduction in the rate on cotton to 0.6 lb ai/acre reduces risk even further. The only concern from the cotton use at 0.6 lb ai/acre is a possible effect to endangered small herbivores. Risk to other mammals is expected to be minimal.

Although cacodylic acid/Na salt is only slightly toxic to laboratory rats, there is some evidence that other mammals, such as the rabbit, may be more sensitive. In a developmental study, pregnant rabbits were dosed for 13 days and observed for adverse effects. At 48 mg/kg/day, all 15 rabbits died by day 29. The NOAEL was 12 mg/kg/day. Depending on the amount of food eaten as a proportion of body weight, the 12 mg/kg/day dose is approximately equivalent to dietary concentrations of 18ppm and 80 ppm for small mammals that consume 66% (herbivores, insectivores) and 15% (granivores) of their body weight per day (see Appendix 4). As can be seen from the EEC tables (see Terrestrial Exposure, Hazard and Risk Section of this document), potential exposure may substantially exceed these concentrations. Graphs depicting residues over time (Appendix 5, Figures 1-14) show that even mean residues exceed this toxic threshold for several weeks.

Terrestrial nontarget plants: Both endangered and non-endangered plants are at risk from applications of cacodylic acid/Na salt. The LOC for non-endangered plants is exceeded only for lowland plants (i.e., those occurring in semi-aquatic habitats) exposed to channelized runoff and drift from noncrop sites. Application to cotton poses minimal risk to non-endangered plants, but endangered species are at risk from drift due to aerial application. That risk is lessened if the maximum application rate is reduced to 0.6 lb ai/A and would be below the endangered species LOC for any rate less than 0.6 lb ai/A. Endangered plants are at greater risk from drift from ground applications at noncrop sites and from channelized runoff from noncrop sites into semi-aquatic sites. Although the LOC is exceeded for a single application, terrestrial plants exposed to only one application may refoliate and recover.

Birds: Cacodylic acid/Na salt is practically nontoxic to birds, and EECs do not approach dose levels that had no adverse acute effects in the avian dietary studies. Reproductive data are not available, but are needed to determine if risk exists at noncrop sites subject to multiple applications. For cotton, reproductive risk should be low, because cacodylic acid/Na salt is applied from August to October, which is after avian breeding seasons.

Aquatic Organisms: Acute LOCs are not exceeded for any aquatic animal or plant. Cacodylic acid/Na salt is assumed to pose minimal acute risk to aquatic organisms. Chronic data are not available but are needed, because cacodylic acid/Na salt is persistent in the aquatic environment.

Human Drinking Water: EFED concludes from monitoring and modeling that *surface* drinking water chronic concentrations originating from cacodylic acid use on cotton at the proposed reduced rate of 0.6 lb/acre straddle the HED threshold of cancer risk. Since natural background concentrations of cacodylic acid also appear to be similar, use of cacodylic acid imposes an additive, localized burden. Ground water should not be impacted incrementally.

ENDANGERED SPECIES CONCERNS

Risk to endangered species is presumed for endangered mammals and terrestrial plants at all use sites. The Agency has developed a program (the “Endangered Species Protection Program”) to identify pesticides whose use may cause adverse impacts on endangered and threatened species, and to implement mitigation measures. At present, the program is being implemented on an interim basis as described in a Federal Register notice (54 FR 27984-28008, July 3, 1989), and is providing information to pesticide users to help them protect these species on a voluntary basis. As currently planned, the final program will call for label modifications referring to required limitations on pesticide uses, typically as depicted in county-specific bulletins or by other site-specific mechanisms as specified by state partners. A final program, which may be altered from the interim program, will be described in a future Federal Register notice. The Agency is not imposing label modifications at this time through the RED. Rather, any requirements for product use modifications will occur in the future under the Endangered Species Protection Program.

ENVIRONMENTAL FATE ASSESSMENT SUMMARY (see Appendix 6 for the full fate assessment, which is indispensable for details, interpretation, and references; and Appendices 7 and 8 for simulation model input and output parameters)

ABSTRACT. Cacodylic acid degrades by aerobic and anaerobic microbial metabolism. Aerobic soil metabolism rates depend critically on ambient conditions, especially soil moisture. Direct abiotic processes are ineffectual. Aerobic soil "half-lives" may range from a few weeks under favorable conditions to several years under dry conditions not conducive to agriculture. The Agency has selected 75 ± 40 days with a standard upper 90% confidence bound on the mean of 103 days (approx. 3-4 months) as an effective aerobic soil half-life. The selected, effective anaerobic (flooded) soil metabolism half-life is 128 ± 38 days with a standard upper 90% confidence bound on the mean of 168 days (approx. 5-6 months). The major metabolites occur in inconstant, variable proportions for unclear reasons. The principal identified metabolites are arsenate, carbon dioxide, and the volatile compounds dimethylarsine and trimethylarsine. Arsenite was not detected under aerobic soil conditions, but would be subject to formation under conditions of its natural occurrence. Methanearsonic acid, if detected, is a minor product. Significant leaching of cacodylic acid or its metabolites to ground water from agricultural use is not expected. Although cacodylic acid has a minor presence in ground water, this cannot be reasonably attributed to labeled agricultural use. Runoff/erosion of applied surface deposits to surface waters and sediments is expected to cause local, temporal perturbations comparable to background concentrations. Surface water monitoring evidence and index drinking water reservoir modeling are similar, and indicate that acute and chronic concentrations for use on cotton (0.6 lb ai/acre) are, respectively, approximately 6 ug/L and 1 ug/L. Bioconcentration or biomagnification of cacodylic acid or metabolites is not indicated.

Introduction and Basis

Cacodylic acid is one of several arsenic containing pesticides which the Agency is, or soon will be, considering for reregistration eligibility. Ultimately, in another action, the Agency will assess the potential overall (aggregate, cumulative) drinking water exposure to these compounds and common transformation products. The EPA Office of Water (OW) is scheduled to issue a proposed and final regulation on the larger issue of "arsenic" in drinking water by the years 2000 and 2001, respectively.

Because of historical toxicological interest in arsenic compounds (the name arsenic has been practically synonymous with "poison" for thousands of years), there is a substantial body of published and unpublished scientific study on their chemistry and environmental fate. Modern literature clearly shows that the biogeochemical interactions of these compounds are complex, and still the subject of active research. However, it is not within the scope of this document to comprehensively review this fascinating area. This has been done to a large extent in the past by the EPA in 1988, the National Academy of Sciences (NAS, 1977), the U.S. Department of the Interior's Fish and Wildlife Service (FWS, 1988), other agencies, individual scientists (e.g., ACS, 1975 Symposium), and very recently by the National Research Council (NRC, 1999; sponsored by EPA) and by the U.S. Geological Survey (USGS, see below). Although the focus here is on *cacodylic acid*, its place in the larger scheme should be understood at the outset.

Essentially all the arsenic since the earth's formation is still present and virtually immutable (barring nuclear transmutation), with new amounts added daily as cosmic dust. Soils, for example, commonly contain from 1-50 parts per million (ppm) of total arsenic in various combined forms, averaging around 5 ppm. Sediments average somewhat higher. Many of the compounds of arsenic, including our subject chemical, cacodylic acid, are synthetically manufactured (ultimately from some primary mineral source) and occur naturally and ubiquitously as well. All are subject to the same fate and transport processes, and are entwined inseparably as part of the global arsenic biogeochemical cycle. Cacodylic acid introduced locally through agriculture cannot be distinguished molecularly from that which is present in the natural background. Only unnaturally high localized concentrations would serve as a telltale. Likewise, other chemical forms of arsenic (organic or inorganic/mineral) resulting from the transformation of cacodylic acid or other arsenic sources which are either naturally present or introduced by human activities (e.g., other pesticides; fossil or wood fuels; agricultural burning; waste incineration; spreading of sewage sludge; poultry and swine manure; mining; smelting; congener contaminant in phosphate detergents and fertilizers; industrial production of semiconductors and glass) cannot, in general, be distinguished as originating exclusively from cacodylic acid. There is certainly much more arsenic in all environmental compartments (air, soil, sediments, water, plants, animals) than could ever be attributed to pesticidal application of cacodylic acid and other arsenicals.

Because of the established complexity, the environmental fate of cacodylic acid and other arsenicals cannot be adequately captured by standard FIFRA, 1988, Guideline studies, which are designed primarily for aspects of xenobiotic organic compounds subjected to a very limited set of experimental conditions. Therefore, in addition to the registrant's FIFRA studies performed under Good Laboratory Practices (GLP), the Agency relies substantially on the open scientific literature, including very recent publications (or some in press), for nuggets of information which directly impact the Office of Pesticide Programs (OPP) environmental fate and effects risk assessment for cacodylic acid. Even so, evidence is often highly variable or seemingly conflicting, indicating that processes, speciation, and environmental interactions (including effects of pH and oxidation-reduction conditions) among the various organic and inorganic species of arsenic are in constant biogeochemical flux and still incompletely understood.

Recent outbreaks of serious arsenic poisoning originating from drinking water wells in India and Bangladesh, as well as those long-established in Taiwan, have attracted the worldwide attention of newspapers and public health officials. Although these events are <u>not</u> associated with use of cacodylic acid, they have had the collateral effect of stimulating renewed scientific interest in the environmental chemistry and fate of arsenicals (Nickson, et al., 1998; Masud, 2000; numerous others). In addition, as will be discussed under the drinking water exposure assessment section of this document, recently completed projects by the USGS and the pending regulation by the EPA Office of Water also attest to the interest in arsenicals in our environment. A better understanding of the many facets of the environmental chemistry and potential risks of environmental arsenic is evolving.

Physicochemical Properties for Cacodylic Acid

EPA PC Code			012501
Chem. Abs. No.			75-60-5
Chemical Names:	**cacodylic acid**, dimethylarsenic acid, hydroxydimethylarsine oxide		
Empirical Formula			$C_2H_7AsO_2$
Molecular Weight			138.0 daltons
Melting Point			192-194 ^{0}C
Solubility in:	water	very soluble	~1 to 3 x 10^6 mg/L
	methanol	very soluble	3.63 x 10^5 mg/L
	hexane		1.02 x 10^{-1} mg/L
Vapor Pressure (Pa)		non-volatile	0
Henry's Law Constant (atm-m^3/mole)		non-volatile	0
Kow			<0.028

Degradation/Metabolism. The Agency is presented with two alternatives (paragraphs 1 and 2 below) for cacodylic acid: the first results from those unpublished studies the registrant submitted under FIFRA and GLP; the second, from published studies the registrant submitted prior to FIFRA, and from other published studies which the Agency selected from the open scientific literature. These studies are documented with references and in greater detail than that given in this summary section in the full fate assessment (Appendix 6) and in individual study summaries (Appendix 10).

1) All environmental fate laboratory studies conducted under current Guidelines (FIFRA, 1988) and GLP criteria ("new studies") showed that cacodylic acid was stable under all tested conditions (see Appendices 6 and 10 for discussion, study summaries, and citations). That is, cacodylic acid did not degrade under the influence of chemical (abiotic), photochemical, or aerobic and anaerobic microbial metabolic processes in soil or water. Thus, on the basis of submitted GLP laboratory results, cacodylic acid would be expected to accumulate indefinitely in the environment at concentrations commensurate with its usage and physical dispersal or transport processes. This is a surprising outcome since cacodylic acid, a component of the earth's natural arsenic cycle[1], has not noticeably accumulated on the planet. The apparent persistence of cacodylic acid in these studies could therefore be an artifact of experimental conditions or undetermined experimental media characteristics such as non-viable soil. Other possibilities are discussed in the fate assessment.

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[1] As part of the arsenic cycle, cacodylic acid is a methylated by-product resulting from, among other things, normal dietary ingestion and metabolism of various arsenic compounds found naturally in food and water. Humans, for example, as an integral part of the global arsenic cycle, convert (primarily in the kidney and liver) much or most of the organic and inorganic arsenicals ingested from natural foods into cacodylic acid which we excrete in our urine (there is extensive literature on this subject).

2) Contrasting with the “new” GLP lab studies, and more consistent with the global picture of the absence of vast accumulations of cacodylic acid, laboratory studies submitted in support of registration prior to establishment of the current, formal Guidelines and GLP criteria (Agency review 27 June 1986, Accession Nos. 259582, 260061, 260782), as well as other studies published in the open technical literature (some more recently than the registrant’s submitted GLP studies: for example, Gao and Burau, 1997), clearly show soil microbial metabolism to be a major route of transformation. This process produced variable proportions of inorganic (mineral) forms of arsenic, carbon dioxide, and volatile organic arsenicals (see below). Supplemental and inconclusive GLP terrestrial field dissipation studies, although suffering from important deficiencies, also add inferential information that cacodylic acid does degrade/metabolize under agricultural conditions at rates adequate to generally avoid significant accumulation over multiple years of application.

None of the published studies strictly meet current Guideline and GLP criteria. However, these studies appeared formally in peer-reviewed scientific publications, as is normal for most scientific work outside of the regulatory process; have been cited in the literature numerous times, including by the NAS, the NRC, and the FWS, and many were submitted by the registrant in the past. These studies provide a body of evidence on the environmental fate of cacodylic acid that cannot be dismissed.

Estimated first-order “half-lives” in aerobic soil have ranged variously from around 20 days to several years, depending in a complex way on soil properties and ambient conditions such as soil moisture, temperature, chemical concentration, and added organic matter. The Agency interpreted and derived results from three published laboratory studies associated with five soils, which together yield an effective average aerobic soil “half-life” of 75 ± 40 days with a standard upper 90% confidence limit on the mean of 103 days (approximately 3-4 months). The average “half-life” in three anaerobic (flooded) soils was 128 ± 38 days with a standard upper 90% confidence limit on the mean of 168 days (approximately 5-6 months). These results stands in opposition to the indeterminately long or “infinite” results from the GLP lab studies.

Why the FIFRA GLP lab results which show cacodylic acid to be stable against metabolism are in stark contrast to all other reported observations (including the absence of accumulating quantities on the planet) is unclear. The registrant did not systematically consider or test several possible experimental factors in an effort to explain the puzzling difference, and thus presents an unresolved environmental fate profile for cacodylic acid. In the attached full fate assessment (Appendix 6) the Agency discusses some of the possible factors which the registrant may have inadvertently not controlled, and which may have led to the apparent stability.

In generating the fate assessment, the Agency has relied primarily upon Alternative 2, and uses published metabolism studies rather than registrant submitted GLP metabolism studies. Alternative 2, the one with significant metabolism, is obviously the more reasonable and compelling. Fortunately, within practical bounds, when combined with ecotoxicity and the nature of transport and exposure to the naturally occurring cacodylic acid and naturally occurring metabolites, there is little difference between the two alternatives in projected ecological effects in the near term. Of course, if cacodylic acid were to continually build up, in accordance with the GLP studies, then effects would mount inevitably and quickly to unacceptable levels. However, with the selected aerobic soil "half-life" of 3-4 months, the asymptotic first-order limit for build up of residual cacodylic acid in soil (without offsite transport) is reached after approximately three successive years of application. At the end of the year which follows the third application, residual cacodylic acid would be 7 to 14% of an amount applied annually. Therefore, immediately following all other successive annual applications, soil amounts would be approximately 107-114% of a single annual amount (100% for the current application + 7-14% for all asymptotic residuals). Arsenic containing transformation products account for the balance of immutable arsenic.

Metabolites. Listed in the box below are the arsenical metabolites discussed herein. It is clear from the published literature that mineral arsenate (AsO_4^{3-}, which is ubiquitous in natural soil) and carbon dioxide are primary aerobic soil metabolites which result from the microbial demethylation of parent cacodylic acid. Volatile organo-arsenic compounds were produced in widely varying proportions in different studies or under different study conditions. These volatiles ranged from less than a fraction of a percent of applied cacodylic acid in some cases, to as high as around 60% in others. In most cases, the exact identities of the trapped volatiles were not individually resolved by the analytical methodologies. In other cases, there was no attempt to trap volatiles, but their existence was inferred indirectly by mass balance difference between total amount of arsenic applied and total remaining arsenic and/or qualitative measures such as odor recognition. Dimethylarsine and trimethylarsine were the consensus as being the most likely among several volatile candidates. These two compounds were specifically identified in significant amounts as they were evolved on laboratory soil and on turf according to at least two published reports.

Noteworthy is that methanearsonic acid, the "obvious" candidate as a potential major degradate, was, when detected, only a very minor product in lab or field soil. [Methanearsonic acid is a non-volatile solid whose sodium salt is the herbicide monosodium methanearsonate (MSMA). It would be produced by loss of one methyl group from cacodylic acid.] In the one available aerobic soil laboratory study where there was analysis for arsenite (AsO_3^{3-}), a possible mineral transformation product, it was not detected. Consistent with this result, and as part of the same study, applied arsenite was converted to arsenate. It is generally accepted and consistent thermodynamically that arsenate rather than arsenite is the prevalent form in aerobic soils. There were no reported tests for arsenite production from cacodylic acid under anaerobic or flooded conditions. However, comparable concentrations of arsenate and arsenite can thermodynamically coexist under certain environmental conditions, including those found in groundwater and surface water; and, indeed, such concentrations have been measured, as will be discussed elsewhere in this document. Ultimate arsenic balance is governed by the summation of shifting proportions of mineral and organic volatile and non-volatile forms.

Arsenic Species Commonly Found in Environmental Samples and Cited Above

“Organic” Species	
$(CH_3)_2AsO(OH)$	**cacodylic acid**, dimethylarsenic acid, hydroxydimethylarsine oxide
$(CH_3)AsO(OH)_2$	methanearsonic acid, methylarsonic acid
$(CH_3)_2AsH$	dimethylarsine
$(CH_3)_3As$	trimethylarsine
“Inorganic” Species	
AsO_4^{3-}	arsenate
AsO_3^{3-}	arsenite

Mobility/Ground Water/Surface Water/Drinking Water

Mobility. Since cacodylic acid is a non-volatile solid and very soluble in water, volatilization of parent is not expected to be a significant route of dispersal. Volatilization of parent was not reported in any lab study.

To fulfill data requirements for mobility in soil, the registrant submitted a published non-FIFRA, non-GLP study for Agency review (part of 27 June 1986 review package, EPA Accession No. 260061). The data was for 16 Mississippi River alluvial flood plain soils. The main study objectives were to correlate sorption with soil properties, and to make direct experimental comparison of the relative sorptions of phosphate (as $H_2PO_4^{1-}$), cacodylic acid/cacodylate[2], arsenate, and methylarsonate (also identified above as methanearsonic acid/ methanearsonate/MSMA). Phosphate, a large magnitude agricultural, industrial, and naturally occurring mineral with established relative immobility, is a well-suited benchmark for comparing the mobility of the suite of arsenicals. (Phosphorous and arsenic are also periodic table congeners in traditional or classical group VA.) The study author did not explicitly calculate sorption coefficients (Kd). From the data, the Agency calculated simple soil Kds for cacodylic acid/cacodylate which ranged from 8.2 to 33 mL/g with a median of 16 mL/g. Sorption did not correlate well with organic matter, but correlated best with clay and iron and aluminum oxide content. In this respect, the organic arsenicals (cacodylic acid and methylarsonate) behaved like the inorganic arsenate and phosphate. By direct comparison with phosphate, the other three chemicals were more strongly sorbed than phosphate in the increasing order:

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[2] Cacodylic acid is a weak acid with a pKa of 6.2. The undissociated acid is in shifting chemical equilibrium with the cacodylate anion, depending on pH. The study author used the salt, sodium cacodylate, and experimentally adjusted the pH to a constant 5.6. At this pH, the molar ratio of cacodylic acid/cacodylate is approximately 3.8/1; at pH 8.5 the ratio is 1/215.

phosphate < cacodylate < arsenate $\underset{\sim}{}$ methylarsonate.

The effect of pH, which was experimentally held constant at 5.6, was not within the design of this study. However, pH could have a major influence on soil sorption because of the anionic/weak acid nature of cacodylate/cacodylic acid (pKa = 6.2, see previous footnote). Generally, anionic (negatively charged) species tend to be less strongly sorbed by soil surfaces which tend to maintain a negative (repelling) charge. The surfaces also tend to become more negative at higher pHs. Thus, at more nearly neutral or alkaline pHs, sorption coefficients could be considerably lower than those given above and mobility correspondingly higher. A study on arsenate (also arsenite) published in 1999 provided some insight on the potential degree of importance of pH on sorption of acid and anion. Although somewhat tenuous because of the changing chemical character of periodic table traditional family group VA elements from non-metal, to metalloid, to metal with increasing atomic number, the above four tested species might be considered a homologous series with the adjacent congeners phosphorus and arsenic at the central core. Therefore, the arsenate data would serve as a relative or surrogate link to the possible effect of pH on the mobility of cacodylic acid/cacodylate.

The 1999 study was on the sorption of arsenic acid/arsenate and arsenious acid/arsenite. The authors measured the sorption dependency on pH and ionic strength for a subset of 4 of 10 Australian soils purposely chosen for their wide variation in characteristics. Sorption showed complex dependencies, with arsenate generally showing *decreased* sorption with *increasing* pH, while arsenite generally showed *increased* sorption with *increasing* pH. The Agency concludes from these surrogate data in the more environmentally relevant range of pHs from 5 to 8.5 and ionic strength of 0.003 molar, that sorption of cacodylate/cacodylic acid should not decrease dramatically with pH when compared to the much larger variability in soil sorption Kds in this and in the previous study with Mississippi flood plain soils.

Ground Water/Drinking Water Exposure (see Appendix 6 full fate assessment for details). Based on the sorption coefficients (Kds) for cacodylic acid, and, more especially, the comparison with the relative immobility of phosphate, any leaching of cacodylic acid to ground water under labeled use conditions (non-point source) would not be expected to be significant. Consistent with these expectations, a supplemental field dissipation study reasonably demonstrated that significant leaching of cacodylic acid should not not occur.

In addition, from extensive survey data the USGS has essentially found no clear correlation with arsenical pesticide use and the presence of *total, unspeciated* arsenic in ground water. The data are based on conventional laboratory analysis which does not differentiate among the various inorganic species and organic species of arsenic. Analysis for *total* or undifferentiated arsenic, of course, gives the summation of arsenic derived from all possible chemical forms and sources, and thus sets an upper limit for the maximum concentration of cacodylic acid (or any other arsenic species). Any contribution specifically from cacodylic acid would be included and masked within the analysis, but not separately identified. A USGS map of the distribution of total arsenic concentrations in groundwater of the U.S. is given in Appendix 11. USGS data for concentration intervals greater than 10 ug/L are not included on this map, but the USGS documents "high" concentrations in excess of 50 ug/L.

Monitoring data specifically for methylated arsenicals such as cacodylic acid are sparse. The sparse groundwater data which do exist for speciated arsenic come from the USGS report, from other recent USGS research studies, and from a study conducted in Florida (see Appendix 6 for details). Unfortunately, speciated sampling occurred only in areas where arsenical pesticides were *not* used. These data, therefore, provide a measure of *baseline* or *background* concentrations. The data suggest that groundwater in areas where arsenical pesticides are <u>*not*</u> applied contains background concentrations of methylated arsenicals $\leq$ 0.4 ug/L (all analyses were below detection limits except for one site with 0.4 ug/L cacodylic acid). *These results and those immediately following are discussed in greater detail in the full fate assessment given as Appendix 6.*

In addition to testing for methylated arsenicals, USGS research scientists also analyzed the same groundwater samples for arsenite and arsenate concentrations. In contrast to the relatively low concentrations of the methylated compounds, concentrations of these mineral forms were much higher. Arsenite or arsenate concentrations each separately ranged from less than the method detection limit of approximately 0.2 ug/L to an exceptionally high 900 ug/L. Their data show that either arsenite or arsenate or both were detected in all samples, typically at 10-50 ug/L. Overall, arsenite and arsenate concentrations were comparable. In a personal communication, one of the study authors expressed surprise at this latter comparability.

<u>Groundwater Conclusion.</u> Based on lab and field fate and transport studies, the Agency concludes that the labeled use (non-point source) of cacodylic acid would not be expected to raise existing background concentrations of cacodylic acid or total arsenic species concentrations in ground water (including natural arsenite and arsenate) more than a small relative fraction over a long period of time. Although the extensive USGS survey report is almost exclusively relevant to total arsenic, and therefore open-ended on cacodylic acid, lack of correlation of total arsenic with pesticide use adds support to the Agency's conclusion. Furthermore, the prevalence of so much natural total arsenic, including arsenite and arsenate, suggests that any concerns be directed toward these other species. While it is patently clear that humans are exposed to significant concentrations of chemical forms of arsenic (including cacodylic acid) in their drinking water from groundwater sources, the labeled use of cacodylic acid should not contribute significantly to the already existing burden from all forms. It is desirable that whenever future groundwater samples are analyzed for total arsenic (as has usually been the case), that arsenic be speciated whenever total arsenic concentrations justify possible toxicity concerns.

<u>Surface Water/Drinking Water Exposure (see Appendix 6 full fate assessment for details).</u> Surface water conclusions are different from the groundwater. In contrast, erosion and runoff of surface deposits would carry cacodylic acid and metabolites to surface waters and sediments at concentrations which could cause local, temporal excursions above background. As discussed below, incremental amounts in some cases appear to be roughly comparable to variable background, and would, therefore,

roughly double ambient concentrations. In drier areas where metabolism would be slower (see attached fate assessment), there could be some build up of cacodylic acid in soil which would accentuate surface water concentrations whenever runoff occurred.

Estimates of environmental excursions above baseline which would be caused by runoff/erosion come from three sources: 1) limited United States Geological Survey (USGS) monitoring data in arsenical pesticide use areas in 1997 for the four arsenic species: cacodylic acid, methane arsenate (equivalent to MSMA), arsenite, and arsenate; 2) a study published in 1973 on the natural background concentrations of the same species around Tampa, Florida, where there was no association with arsenical pesticide use; and, for comparison, 3) computer simulation modeling. These three sources are considered sequentially below. The BASINS and STORET databases maintained by the US EPA provided a large body of data (many tens of thousands or more of entries) on *total* arsenic concentrations in surface waters of the U.S. However, because of the wide ranging concentrations (in some cases, approximately in the parts per million range) in space and time, and the multiplicity of possible major sources of arsenic, any attempt to associate these with cacodylic acid use would likely be a fruitless exercise, and would certainly require a major resource effort akin to that by the USGS for groundwater.

1) USGS sampling data. USGS research scientists collected surface water samples at one or two week intervals from early March through the middle of September of 1997 from each of three sites associated with different basins or sub-basins in an agricultural region potentially impacted by application of MSMA (application is normally from May through July). MSMA can be used as a surrogate for cacodylic acid because it is chemically closely related to cacodylic acid; produces cacodylic acid as a metabolite, and may itself be a minor metabolite of cacodylic acid; and has a similar use and environmental fate profile (cacodylic acid is slightly more mobile). A total of 24 samples were analyzed from each site. The scientists had no baseline data for "pristine" areas. Analyses were for MSMA (as the acid MMA, where the amount of MSMA $\underset{\sim}{}$ 1.2 x MMA); cacodylic acid (as itself, abbreviated as DMA); arsenite (As^{3+}); and arsenate (As^{5+}). *Maximum concentrations of MMA at the three sites were approximately 2, 3, and 5 ug/L (parts per billion), and were relatively short-lived. As a surrogate, for similar application rates, similar concentrations (multiply by 1.1) would be expected for cacodylic acid had it been used in the area rather than MSMA.* Although it was apparently not in use, concentrations of cacodylic acid, a possible metabolite of MSMA, were at or below the detection limit of 0.2 ug/L, except for one sample which registered approximately 0.6 ug/L.

Maximum surface water arsenite concentrations were approximately 2, 3, and 3 ug/L. Maximum arsenate concentrations were approximately 2, 5.5, and 5.5 ug/L. The comparable concentrations of arsenite and arsenate is noteworthy, since the USGS scientists, *a priori*, expected relatively little arsenite. These inorganic species generally increased later in the summer, possibly indicating alkylarsenic degradation (oxidation) or a secondary source of inorganic arsenic. However, until similar baseline data for surface water sources in a similar area where no arsenicals are applied are compared, no conclusions can be reached about whether the fluctuations are part of the natural arsenic cycle or influenced by pesticide application. *Nevertheless, regardless of the source or the mechanism, the presence of all these arsenicals should be included as part of any overall exposure assessment.*

2) Sampling for the study published in 1973 was for 10 natural waters in the vicinity of Tampa, Florida. There were six surface fresh water bodies (two rivers, two ponds, two lakes), three saline waters (two bays, one tidal flat), and one water well at a remote camping area. Tampa tap water was also analyzed. Analysis was for the same four arsenic species: cacodylic acid (dimethylarsenic acid), methylarsonic acid (methyl arsonate, MMA or MSMA), arsenite, and arsenate. Presumably, all water sites were sampled once with two or more replicates analyzed; however, the study authors did not report specifics on sampling dates and the number of samples analyzed. *All concentrations reported below are as arsenic equivalents unless otherwise indicated* (to get cacodylic acid concentrations, for example, multiply all values given below for the arsenic equivalent of cacodylic acid by the relative chemical weights of approximately 138/75 or 1.8). [In addition to the water samples, human urine (15 ppb cacodylic acid, N=8; 3 ppb methylarsonic acid, N=8; 2 ppb arsenite, N=4; and 4 ppb arsenate, N=4), bird eggshells, seashells, and a limestone rock, were analyzed.]

Concentrations of cacodylic acid (reported as arsenic) in the natural waters ranged up to 1.0 ppb (1.0 x 1.8 = 1.8 ppb cacodylic acid). At one site, the Hillsborough River, concentrations were below a remarkably low detection limit of 0.02 ppb, while the median value for cacodylic acid (as arsenic) at the other nine sites was approximately 0.3 ppb (0.5 ppb cacodylic acid). The well water concentration was 0.2 ppb (0.4 ppb cacodylic acid). Concentrations of arsenate, detected at all ten sites, were similar to cacodylic acid. Arsenite was detected at only six of the ten sites, but had the highest concentration (2.7 ppb) of all species. Methylarsonic acid, detected in eight of the ten sites, was generally present at lower concentrations, the highest being 0.22 ppb. Total arsenic concentrations ranged from approximately 0.3 to 3.6 ppb. The extent to which these concentrations represent the natural background or baseline in the Tampa area or are influenced by introduction of artificial sources is unknown. However, the study authors considered the sampled sites as “natural” waters. Tampa tap water “contained only traces of arsenate”.

3) It is informative to compare the preceding measured results use areas (1 above) and non-use areas (2 above) with environmental simulation model predictions. For this purpose, the Agency has used two adaptations of the same model, one for estimates of drinking water concentrations in surface sources, the other for estimates of ecological exposure to aquatic organisms. Predictions of ecological exposure are considered elsewhere in this document.

For surface drinking water, the Agency has recently adapted the standard PRZM/EXAMS model to estimate runoff to an Index Drinking Water Reservoir (IR), and also makes an allowance for the portion of surrounding land which may be cropped. Resulting acute and chronic drinking water concentrations for cacodylic acid for the IR scenario for cotton grown in Mississippi with one annual application of cacodylic acid at a rate of 0.60 lb/acre and with a multiplicative factor for percent cropped area (PCA) of 0.20 (20% cropped) are:

Acute (one-in-ten year peak concentration x PCA): 29 ug/L x 0.20 ~ 6 ug/L (ppb)

Chronic (one-in-ten year peak concentration x PCA): 7.0 ug/L x 0.20 ~ 1 ug/L (ppb)

Conclusion for Surface Drinking Water. Whether coincidence or not, and whatever the source, the modeled values for cacodylic acid for surface drinking water are similar to those measured and discussed above for both use and non-use areas, and would, therefore, generally represent an additional, localized burden above background. If there are toxicological concerns at or near the monitored and modeled concentrations, then, clearly, this observation invites broader scale, systematic environmental sampling and analysis for cacodylic acid (and other speciated arsenicals) in order to determine statistically the associations, ranges of exposure, and possible effects. Adequate analytical methods for arsenical chemical speciation are readily available.

Bioconcentration. A low octanol/water partitioning ratio (Kow < 0.028) indicates little potential for bioconcentration of cacodylic acid. Although the scientific literature (FWS, 1988; NAS, 1977; ACS, 1975) shows that many plant and animal species (shrimp, for example) selectively have high bioconcentration factors for other organic forms of arsenic, these compounds are reported as practically nontoxic. In many species (including humans), cacodylic acid is a major, final waste product from the metabolism of arsenic compounds ingested from natural food, minerals, and water sources. The published literature also shows the absence of biomagnification of arsenic.

AQUATIC EXPOSURE, HAZARD AND RISK

Aquatic Hazard Data

Toxicity to Freshwater Organisms:

Six studies using five test species are available to establish the acute toxicity of cacodylic acid/Na salt to fish and aquatic invertebrates. These species were rainbow trout (*Oncorhynchus mykiss*), bluegill sunfish (*Lepomis macrochirus*), water flea (*Daphnia magna*), grass shrimp (*Palaemonetes kadiakensis*), and scud (*Gammarus fasciatus*). Results of these tests are tabulated below.

Freshwater Fish and Invertebrate Toxicity

Test Species	% ai	Test Conditions	LC50 (ppm)	Toxicity Category	MRID No.	Study Classification
Bluegill	29.4 *	flow-through	>133	practically nontoxic	417483-02	core
Bluegill	100 (acid)	static	17	slightly toxic	400980-01	core
Rainbow trout	29.4 *	flow-through	>152	practically nontoxic	417483-01	core
Water flea	29.4 *	flow-through	61.6 18.1[1]	slightly toxic	417479-01	core
Glass shrimp	100 (acid)	static	28	slightly toxic	400980-01	supplemental
Scud	100 (acid)	static	135	practically nontoxic	400980-01	supplemental

* the material tested (Cacodylate 3.25) is 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

[1] adjusted LC50 based on the purity of the test material

Chronic data were not submitted. Because cacodylic acid/Na salt has a long residence time in the aquatic environment and because aquatic EECs for the highest application rates on noncrop sites are greater than 0.01 of the LC50s, data are needed to assess chronic risk. An aquatic invertebrate life-cyle test (72-4b), using the water flea as the test species, is required to support the highest application rates on noncrop sites.

Toxicity to Estuarine/Marine Organisms:

Six studies are available for assessing the acute toxicity of cacodylic acid/Na salt to estuarine/marine organisms. Test species were the sheepshead minnow (*Cyprinodon variegatus*), longnose killifish (*Fundulus similis*), mysid shrimp (*Americamysis bahia*), Eastern oyster (*Crassostrea virginica*), and pink shrimp (*Penaeus durorarum*). Test results are presented below.

Estuarine/marine Fish and Invertebrate Toxicity

Test Species	% ai	Test Conditions	LC50/EC50 (ppm)	Toxicity Category	MRID No.	Study Classification
Sheepshead minnow	29.4*	static	990 / 291[1]	practically nontoxic	424333-01	core
Longnose killifish	98 (acid)	static	>40	not determined	402284-01	supplemental
Mysid shrimp	29.4*	static	33 / 9.7[1]	moderately toxic	424333-02	core
Eastern oyster	29.4*	flow-through	>110	practically nontoxic	424681-01	core
Eastern oyster	98 (acid)	flow-through	>1	not determined	402284-01	supplemental
Pink shrimp	98 (acid)	static	>40	not determined	402284-01	supplemental

* the material tested (Cacodylate 3.25) is 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

[1] adjusted for the purity of the test material

Toxicity to Aquatic Plants:

Tier II tests were submitted to establish the toxicity of cacodylic acid/Na salt to aquatic plants. Test species were duckweed (*Lemna gibba*), a vascular species, and four non-vascular species: green algae (*Kirchneria subcapitata*), marine diatom (*Skeletonema costatum*), freshwater diatom (*Navicula pelliculosa*), and blue-green algae (*Anabaena flos-aquae*). Test results are tabulated below.

Nontarget Aquatic Plant Toxicity [1]

Test Species	EC50 (ppm)	NOAEL (ppm)	MRID No.	Study Classification
Vascular species:				
Duckweed	30.9	2.4	417911-05	core
non-Vascular species:				
Green algae	96.2	<67	417911-01	core
Marine diatom	56.2	9.8	417911-04	core
Freshwater diatom	17.1	13.6	417911-03	core
Blue-green algae	44.7	24.6	417911-02	core

[1] the test material (Cacodylate 3.25) is 4.9% acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

Risks to Aquatic Animals:

Acute RQs using maximum EECs and the most sensitive test species are tabulated below for freshwater and estuarine/marine fish and aquatic invertebrates. The given EECs are screening estimates based on the Agency's GENEEC simulation model. An example of a GENEEC input/output table is given in Appendix 6 for a single application to cotton at the proposed, reduced use rate of 0.6 lb ai/acre (not tabulated below).

Acute Risk Quotients for Fish and Aquatic Invertebrates

Site	Appl. Rate (lb ai/A)	No. Appl.	Peak EEC (ppb)	Acute RQ[1] - Freshwater		Acute RQ[1] - Estuarine/marine	
				Fish[2]	Invertebrate[3]	Fish[4]	Invertebrate[5]
Cotton	1.2	1	21	<0.01	<0.01	<0.01	<0.01
Noncrop areas	8.1	3	403	0.02	0.02	0.01	0.04
Orchard (understory)	5.0	3	248	0.01	0.01	<0.01	0.03

[1] RQ = EEC/LC50 (fish) or EC50 (invertebrates)
[2] LC50 = 17 ppm (bluegill)
[3] EC50 = 18.1 ppm (water flea)
[4] LC50 = 40 ppm (killifish)
[5] EC50 = 9.7 ppm (mysid)

Minimal acute risks are presumed for freshwater and estuarine/marine aquatic animals. No acute risk LOC is exceeded at any use site even for the highest application rates. Chronic risk cannot be assessed until data are submitted.

Risks to Aquatic Plants:

RQs for aquatic plants are tabulated below. RQs for non-endangered species are based on the duckweed EC50 for vascular species and the EC50 for the freshwater diatom, the most sensitive non-vascular species tested. Risk to endangered vascular species is based on the duckweed NOAEL. Again, the given EECs are screening estimates based on the Agency's GENEEC simulation model, and are the same as in the table above. Appendix 6 gives the example of a GENEEC input/output table for a single application to cotton at the proposed, reduced use rate of 0.6 lb ai/acre (not tabulated below).

Risk Quotients for Aquatic Plants

Site	Appl. Rate (lb ai/A)	No. Appl.	Peak EEC (ppb)	RQ[1,2]		
				non-endangered vascular spp.	non-endangered non-vascular spp.	endangered vascular spp.
Cotton	1.2	1	21	<1	<1	<1
Noncrop areas	8.1	3	403	<1	<1	<1
Orchard (understory)	5.0	3	248	<1	<1	<1

[1] RQ = EEC / EC50 (non-endangered species) or NOAEL (endangered species)

[2] the vascular (duckweed) EC50 =30.9 ppm and NOAEL = 2.4 ppm; the non-vascular freshwater diatom EC50 = 17.1 ppm

LOCs are not exceeded for aquatic plants. Minimal risk is presumed for either endangered or non-endangered species from any use site.

TERRESTRIAL EXPOSURE, HAZARD AND RISK

Terrestrial Exposure Assessment:

EECs for Birds and Mammals

The estimated environmental concentrations (EECs) on potential bird and mammal food items are based on Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994). Based on their findings, a 1 lb ai/acre pesticide application is presumed to provide the following maximum and mean EECs: 240 and 85 ppm for short grass; 135 and 45 ppm for broad-leaved plants; and 15 and 7 ppm for seeds, pods, and fruits. Residue data are not available for insects; estimates are based on an assumption that larger insects have a similar surface area to volume ratio as the foliage of broad-leaved plants and thus may have similar residues if directly sprayed. For short grass, no accumulation is assumed between applications, because cacodylic acid/Na salt dessicates green vegetation within 5 to 7 days. However, some accumulation may occur on food items such as insects or seeds exposed within the treated area. The maximum residues likely to occur on insects and seeds immediately after the final application are estimated using the maximum EECs from Kenega and first-order kinetics for dissipation (see Appendix 3 for residue estimation method). Because a foliar dissipation value is not available, a default half-life of 30 days is assumed. The interval between applications is not specified on labels but is assumed to be 14 days. Predicted maximum EECs for each use site are tabulated below. For noncrop areas and orchard understory, EECs are calculated for both multiple and single applications.

EECs on Avian and Mammalian Food Items

Site	Max. Appl. Rates (lb ai/A)	No. Appl.	Predicted Maximum EEC (ppm) on Food items		
			Short grass[1]	Insects[2]	Seeds[2]
Cotton	1.2	1	288	162	18
Cotton[3]	0.6	1	144	81	9
Noncrop areas	2.5	3	600	758	84
	8.1	3	1944	2457	273
Noncrop areas	8.1	1	1944	1093	121
Orchard (understory)	0.2	3	48	60	7
	5.0	3	1200	1516	168
Orchard (understory)	5.0	1	1200	675	75

[1] because cacodylic acid is a desiccant, residues are not expected to accumulate between applications on grass; therefore, peak residues on short grass are the same for single and multiple applications

[2] maximum residues on insects and seeds are the highest residues likely to occur immediately after the final application, assuming a 30-day halflife

[3] EECs for the proposed reduction in the maximum application rate for cotton are included for the assessment

EECs for Terrestrial Plants

Terrestrial plants growing near treatment sites may be exposed to pesticides from runoff and spray drift. Upland areas located adjacent to treatment sites are assumed to receive sheet runoff from one treated acre onto one untreated acre after each application. Lowland habitats (i.e., semi-aquatic areas) are assumed to receive channelized runoff from 10 treated acres onto 1 untreated acre. The amount of pesticide to which nontarget plants are potentially exposed depends on the application rate, method of application (ground or air), and the pesticide's solubility in water. The amount of active ingredient that runs off is presumed to be a proportion of the application rate: 1%, 2%, or 5% for water solubility values of <10 ppm, 10-100 ppm, and >100 ppm, respectively. For cacodylic acid/Na salt, a runoff value of 5% is presumed, based on solubility values that exceed 100 ppm in water. Drift from ground-spray and aerial applications are assumed to be 1% and 5%, respectively, of the application rate. An application efficiency of 75% also is assumed for aerial application. Formulas for calculating runoff and drift onto off-site areas are presented in Appendix 2.

EECs for dry and semi-aquatic off-site areas are tabulated below for a single application.

Terrestrial Plant EECs From a Single Spray Application

Chemical/ Site	Appl. Rate (lb ai/A)	Appl. Method	Runoff (lb ai/A)		Drift (lb ai/A)	Total Load (lb ai/A)	
			Sheet	Channelized		Upland[1]	Semi-aquatic[2]
Cotton	1.2	ground	0.06	0.61	0.01	0.07	0.62
		aerial	0.05	0.46	0.06	0.11	0.52
Cotton[3]	0.6	ground	0.03	0.30	0.01	0.04	0.32
		aerial	0.02	0.23	0.03	0.05	0.26
Noncrop areas	8.1	ground	0.41	4.05	0.08	0.49	4.13
	2.5	ground	0.13	1.25	0.03	0.15	1.28
Orchard (understory)	5.0	ground	0.25	2.50	0.05	0.30	2.55
	0.2	ground	0.01	0.10	<0.01	0.01	0.10

[1] sheet runoff plus drift

[2] channelized runoff plus drift

[3] provided to show exposure and risk from a proposed lower application rate for cotton

Toxicity to Birds:

One acute oral and two dietary toxicity studies were submitted to establish the acute and subacute toxicity of cacodylic acid/Na salt to birds. Two reproductive studies are required, but have not been submitted. Test species are the northern bobwhite (*Colinus virginianus*) and the mallard (*Anas platyrhynchos*). Test results are tabulated below.

Avian Toxicity

Test species	Test	% ai Tested	Toxicity Value	Toxicity Category	MRID No.	Study Classification
Northern bobwhite	Acute oral	29.4*	LD50 >2250 mg/kg	practically nontoxic	416083-04	core
Northern bobwhite	Dietary	99.95 (acid)	LC50 >5620 ppm	practically nontoxic	425513-01	core
Mallard	Dietary	99.95 (acid)	LC50 >5620 ppm	practically nontoxic	425513-02	core
Northern bobwhite	Reproduction		no data			outstanding
Mallard	Reproduction		no data			outstanding

* the material tested (Cacodylate 3.25) is 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

Avian reproduction studies (71-4a,b) are required to support multiple applications on noncrop sites.

Toxicity to Mammals

The Agency uses laboratory rat (*Rattus norvegicus*) or laboratory mouse (*Mus musculus*) and any other relevant toxicity information from studies required by the Agency's Health Effects Division (HED) for the assessment for wild mammals. The toxicity data for cacodylic acid/Na salt are tabulated below.

Mammalian Toxicity

Test species	Test type	% ai	Toxicity	Affected endpoints	MRID No.
Laboratory rat	acute oral	29.4*	LD50 = 2800 mg/kg 823[1]	mortality	419256-01
Laboratory rat	two-generation reproductive	98.7 (acid)	NOAEL = 147 ppm[2]	none	410595-01 and 416522-01
Rabbit	developmental	99.8 (acid)	NOAEL = 12 mg/kg/day[3] LOAEL = 48 mg/kg/day	mortality, abortions, body-wt loss, reduced food consumption	40663301

* the material tested (Cacodylate 3.25) contains 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

[1] adjusted for the purity of the test material

[2] the highest dose tested

[3] dietary concentration equivalent to an NOAEL of 12 mg/kg/day would be about 18 ppm for herbivores and insectivores and 80 ppm for granivores (see attachment)

The adjusted acute oral toxicity value categorizes Cacodylate 3.25 as slightly toxic to small mammals. EFED is also including results from two HED studies that provide information on the effects of short-term exposure to mammals. Cacodylic acid did not cause reproductive effects in rats dosed at 0, 3, 21 or 147 ppm or exhibit detrimental developmental effects in their offspring during a two-generation reproduction study. *However, adverse effects were observed in a developmental study when groups of pregnant New Zealand white rabbits were dosed (gavage) at levels of 0, 3, 12 or 48 mg/kg/day for 13 days (days 7 to 19 of gestation). At 48 mg/kg/day (equivalent to a dietary concentration of about 18 ppm; see Appendix 4), all 15 rabbits died by day 29, and 9 of the 15 aborted fetuses prior to death. Body weight, weight gain, and food consumption also were greatly reduced prior to death. HED concluded that such effects might occur even from a single dose.*

Toxicity to Insects

An acute contact study was submitted to establish the toxicity of cacodylic acid/Na salt to the honey bee (*Apis mellifera)*. The toxicity data are used for recommending appropriate label precautions for beneficial insects. Test results are tabulated below.

Beneficial Insect Toxicity

Test species	% ai	LD50 (µg/bee)	Toxicity Category	MRID No.	Study Classification
Honey bee	29.4*	>100	practically nontoxic	416083-10	core

* the material tested (Cacodylate 3.25) contains 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

Because Cacodylate 3.25 is practically nontoxic to the honey bee, precautionary labeling for beneficial insects is not required.

Toxicity to Terrestrial Plants:

Two studies were submitted to determine the toxicity of cacodylic acid/Na salt to terrestrial nontarget plants. The studies include a Tier II seedling emergence test with 10 species and a Tier II vegetative vigor test with 10 species. Test species must include the following: six species, including soybean (*Glycine max*) and a root crop, from at least four dicotyledonous families; and four species, including corn (*Zea mays*), from at least two monocotyledonous families. Test results are presented in the following table:

Nontarget Terrestrial Plant Toxicity[1]

	Seedling Emergence[2]			Vegetative Vigor[3]		
Test Species	Endpoint Affected[4]	EC25 (l b ai/A)	NOAEL (lb ai/A)	Endpoint Affected[4]	EC25 (l b ai/A)	NOAEL (lb ai/A)
monocots:						
Corn	plant height	3.48	1.34[5]	dry weight	1.05	0.67
Oat	dry weight	5.70	5.36	dry weight	0.42	0.03
Onion	emergence	3.75	5.36[6]	dry weight	0.56	0.67[5]
Ryegrass	emergence	3.90	1.34[5]	dry weight	0.79	0.67
dicots:						
Carrot	none	>21.45	21.45	dry weight	0.73	0.67
Soybean	dry weight	2.20	1.34	dry weight	0.33	0.25
Tomato	plant height	7.18	2.68[5]	dry weight	0.41	0.67[6]
Cabbage	dry weight	0.92	0.67	dry weight	0.12	0.03
Cucumber	dry weight	2.38	1.34	dry weight	0.80	0.67
Lettuce	dry weight	4.87	5.36[6]	dry weight	0.21	0.25[6]

[1] the test material (Cacodylate 3.25) is 4.9% cacodylic acid and 28.4% Na salt (29.4% total cacodylic acid equivalent)

[2] MRID No. 417323-01 (core)

[3] MRID No. 417323-02 (core)

[4] only the most sensitive endpoint has been tabulated for each species

[5] based on phytotoxicity

[6] NOAEL values exceeded EC25 values because of variability between replicate means

Cabbage, a dicot, is the most sensitive species tested for both seedling emergence and vegetative vigor.

Risks to Birds:

Minimal acute risk is presumed, because cacodylic acid/Na salt is practically nontoxic to birds (LC50 >5620 ppm) and maximum residues on avian food items are not expected to exceed 1944 ppm at any use site. No avian reproduction data are available. The lack of avian reproduction data leads to uncertainty in concluding that birds are not at risk from registered uses of cacodylic acid/Na salt at noncrop sites. Reproductive risk is probably low from cotton use, because cacodylic acid is applied in most regions from August to October, after most birds have finished breeding.

Risks to Mammals:

Acute RQs are tabulated below for small mammals. The EECs used to calculate RQs for herbivores are based on a single application, even though some labels permit multiple applications. Green vegetation receiving high doses of cacodylic acid will dessicate between applications. For screening purposes, residues on insects and seeds might accumulate with repeat applications. Therefore the maximum residue is that which might occur immediately following the final application assuming the residues from previous applications partially, but not completely, dissipate between treatments. Since no terrestrial dissipation information is available, a default half-life life of 30 days is used.

Small Mammal Acute Risk Quotients

Site	Appl. Rate (lb ai/A)	No. appl.	EEC (ppm)			Acute RQ[1,2]		
			Grass	Insects	Seeds	Herbivores[3]	Insectivores[3]	Granivores[4]
Cotton	1.2	1	288	162	18	0.2 **	0.1 *	<0.1
Cotton[5]	0.6	1	144	81	9	0.1 *	<0.1	<0.1
Noncrop areas	2.5	3	600	758	84	0.5 ***	0.6 ***	<0.1
	8.1	3	1944	2457	273	1.6 ***	1.9 ***	<0.1
Noncrop	8.1	1	1944	1093	121	1.6***	0.8 ***	<0.1
Orchard (understory)	0.2	3	48	60	6.7	<0.1	<0.1	<0.1
	5.0	3	1200	1516	168	1.0 ***	1.2 ***	<0.1

[1] RQ = EEC / [LD50 / food eaten expressed as % of bw]
[2] LD50 = 823 mg/kg (lab. rat)
[3] for a 35-g herbivore or insectivore (mammal) that consumes an amount of green vegetation or insects equivalent to 66% of its body weight
[4] for a 35-g granivore (mammal) that consumes an amount of seeds equivalent to 15% of its body weight
[5] cotton use at 0.6 lb ai/acre was assessed to show possible risk at a proposed lower application rate
[6] exposure and risk for a single application provided for comparison purposes, and to show benefit of reducing number of applications
*** exceeds the LOCs for high risk (RQ ≥0.5), restricted use (RQ ≥0.2), and endangered species (RQ ≥0.1)
** exceeds the LOCs for restricted use and endangered species
* exceeds the LOC for endangered species

High risk is presumed for small mammals (herbivores and insectivores) where cacodylic acid/Na salt is used to control weeds at noncrop sites and in orchards. The restricted use and endangered species LOCs are exceeded for all use sites, including the maximum labeled rate for cotton. Only the endangered species LOC is exceeded, and only for herbivores, for the proposed maximum rate of 0.6 lb ai/A on cotton. Granivorous mammals are not presumed at risk at any site.

The Agency is also assessing potential risk based on the responses of pregnant rabbits in a developmental study from which an NOAEL of 12 mg/kg/day was derived. The effects at the next higher dose level, 48 mg/kg/day, included 100% mortality by day 29. A daily dose of 12 mg/kg/day is approximately equivalent to a dietary concentration of 18 ppm and 80 ppm for mammals that consume an amount of food equivalent to 66% (herbivores and insectivores) and 15% (granivores) of their body weight per day, respectively (see Appendix 4). Comparing the

NOAEL with the EECs tabulated above, high risk is presumed for herbivores, insectivores, and granivores at all use sites (see also graphs in Appendix 5).

Risks to Nontarget Terrestrial Plants:

RQs for non-endangered and endangered terrestrial plants inhabiting upland and semi-aquatic areas are presented in the following two tables. The seedling emergence EC25 (non-endangered species) or NOAEL (endangered species) is used in the risk calculations based on total loading on upland and lowland sites, whereas the vegetative vigor values are used to assess risk to plants exposed only to drift.

Risk Quotients for non-Endangered Terrestrial Plants From a Single Application

Site	Appl. Rate (lb ai/A)	Appl. Method	Total Loading (lb ai/A)		Drift (lb ai/A)	RQ[3,4]		
			Upland[1]	Lowland[2]		Upland	Lowland	Drift
Cotton	1.2	ground	0.07	0.62	0.01	<1	<1	<1
		aerial	0.11	0.52	0.06	<1	<1	<1
Cotton[5]	0.6	ground	0.04	0.31	0.01	<1	<1	<1
		aerial	0.05	0.26	0.03	<1	<1	<1
Noncrop areas	2.5	ground	0.15	1.28	0.03	<1	1.4 *	<1
	8.1	ground	0.49	4.13	0.08	<1	4.5 *	<1
Orchard (understory)	0.2	ground	0.01	0.10	<0.01	<1	<1	<1
	5.0	ground	0.30	2.55	0.05	<1	2.8 *	<1

[1] sheet runoff and drift

[2] channelized runoff and drift

[3] RQ = lb ai/A / EC25 (seedling emergence for total loading and vegetative vigor for drift)

[4] Seedling emergence EC25s = 0.92 lb ai/A; vegetative vigor EC25 = 0.12 lb ai/A

[5] provided to show risk quotients from a proposed lower application rate for cotton

* exceeds the LOC (RQ $\geq$1) for nontarget plants

Risk is presumed for non-endangered plants inhabiting lowland areas that receive channelized runoff and drift (i.e., total loading) from a single application to noncrop and orchard sites. Risk from a single application is probably low, because terrestrial plants likely will refoliate after a single exposure. Repeat applications are likely to pose more risk. Risk from application to cotton is expected to be minimal.

Risk Quotients for Endangered Terrestrial Plants From a Single Application

Site	Appl. Rate (lb ai/A)	Appl. Method	Total Loading (lb ai/A)		Drift (lb ai/A)	RQ[3,4]		
			Upland[1]	Lowland[2]		Upland	Lowland	Drift
Cotton	1.2	ground	0.073	0.621	0.012	<1	<1	<1
		aerial	0.107	0.518	0.061	<1	<1	2 *
Cotton[5]	0.6	ground	0.036	0.31	0.006	<1	<1	<1
		aerial	0.053	0.259	0.03	<1	<1	1 *
Noncrop areas	2.5	ground	0.150	1.275	0.025	<1	1.9 *	<1
	8.1	ground	0.486	4.132	0.081	<1	6.2 *	2.7 *
Orchard (understory)	0.2	ground	0.012	0.102	0.002	<1	<1	<1
	5.0	ground	0.300	2.550	0.05	<1	3.8 *	1.7 *

[1] sheet runoff and drift

[2] channelized runoff and drift

[3] RQ = lb ai/A / NOAEL (seedling emergence for total loading and vegetative vigor for drift)

[4] Seedling emergence NOAEL = 0.67 lb ai/A; vegetative vigor NOAEL = 0.03 lb ai/A

[5] provided to show risk quotients from a proposed lower application rate for cotton

* exceeds the LOC (RQ ≥1) for nontarget plants

Risk is presumed for endangered plants inhabiting lowland areas exposed to runoff and drift (i.e., total loading) from a single application to noncrop and orchard sites (highest application rates). Endangered plants exposed to drift from aerial application to cotton are also at risk. Risk from drift alone in areas not subject to runoff is also expected from the highest application rates on noncrop areas and in orchards. Repeat applications are likely to increase these risks.

APPENDIX 1

DEFINITIONS AND EXPLANATIONS OF TERMS AND ACRONYMS

RISK QUOTIENTS AND LEVELS OF CONCERN

Risk quotients (RQs) are compared to levels of concern (LOCs) to assess the potential for adverse ecological effects to nontarget organisms. An RQ is an index comparing estimated environmental concentrations (EECs) with the most sensitive ecotoxicity values, where

RQ = EEC / TOXICITY

Risk presumptions are made by comparing acute and chronic RQs to LOCs for birds, mammals, plants, and aquatic organisms. Exceedance of an LOC indicates the potential for serious risk to nontarget organisms and the need for the Agency to consider regulatory action. LOCs address the following risk presumption categories:

acute high risk: regulatory action may be warranted to eliminate or reduce risk;
acute restricted use: risk may be mitigated by restricted use classification;
acute endangered species: regulatory action may be warranted to protect endangered species; and
reproductive and chronic risk: regulatory action may be warranted to eliminate or reduce reproductive or chronic risk.

The ecotoxicity values for acute effects are:

LC50: birds and fish
LD50: mammals
EC50: aquatic plants and aquatic invertebrates
EC25: terrestrial plants
NOAEL: endangered terrestrial and aquatic plants

The NOAEL is the ecotoxicity value for reproductive and chronic effects for birds, mammals, fish, and aquatic invertebrates.

Risk presumptions are tabulated below.

Risk Presumption	RQ	LOC
Birds and Mammals		
Acute High Risk	EEC[1]/LC50 or LD50/sqft[2] or LD50/day[3]	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Reproductive Risk	EEC/NOAEL	1
Aquatic Animals		
Acute High Risk	EEC[4]/LC50 or EC50	0.5
Acute Restricted Use	EEC/LC50 or EC50	0.1
Acute Endangered Species	EEC/LC50 or EC50	0.05
Chronic Risk	EEC/NOAEL	1
Plants		
Acute Risk	EEC[5]/EC25 (terrestrial) or EEC[4]/ EC50 (aquatic)	1
Endangered Species	EEC/EC05 or NOAEL	1

[1] ppm ai on avian and mammalian food items (grass, insects, seeds)
[2] mg ai per ft^2 ÷ [LD50 * animal wt (kg)]
[3] mg ai consumed per day ÷ [LD50 * animal wt (kg)]
[4] aquatic concentration of ai
[5] lb ai/A

APPENDIX 2

FORMULAS FOR OFF-SITE TERRESTRIAL PLANT EXPOSURE

EECs for Terrestrial Plants Inhabiting Upland Areas Adjacent to Treatment Sites

Ground application:

Runoff = maximum application rate (lb ai/A) x runoff value (1%, 2%, or 5%)
Drift = maximum application rate (lb ai/A) x 1% (drift)
Total Loading = runoff (lb ai/A) + drift (lb ai/A)

Aerial application:

Runoff = max. appl. rate (lb ai/A) x 75% (application efficiency) x runoff value
Drift = max. appl. rate (lb ai/A) x 5% (drift)
Total Loading = runoff (lb ai/A) + drift (lb ai/A)

EECs for Terrestrial Plants Inhabiting Lowland Areas

Ground application:

Runoff = max. appl. rate (lb ai/A) x runoff value x 10 acres
Drift = max. appl. rate x 1%
Total Loading = runoff (lb ai/A) + drift (lb ai/A)

Aerial application:

Runoff = max. appl. rate (lb ai/acre) x 75% x runoff value x 10 acres
Drift = max. appl. rate (lb ai/A) x 5%
Total Loading = runoff (lb ai/A) + drift (lb ai/A)

APPENDIX 3

ESTIMATING RESIDUES ON TERRESTRIAL FOOD ITEMS

The Agency estimates the residues on terrestrial food items from multiple applications and over time by taking into account:

- application rate for a single application,
- number of applications,
- application interval, and
- dissipation rate

The model of Hoerger and Kenega (1972), as modified by Fletcher *et al.* (1994) was used to estimate pesticide concentrations on selected avian or mammalian food items. This model predicts the maximum concentrations that may occur immediately following a direct application at 1 lb ai/A. For 1 lb ai/A applications, concentrations on short grass, broadleaf plants, and fruits are predicted to be 240 and 85 ppm, 135 and 45 ppm, and 15 and 7 ppm for maximum and mean residues, respectively. The predicted maximum concentration for broadleaf plants and fruits are used to represent maximum concentrations that may occur on small and large insects, respectively. Linear extrapolation is then used to estimate maximum terrestrial EEC's for single applications at other application rates.

The Agency uses this as a screening level exposure assessment tool to determine peak terrestrial EECs resulting from multiple applications. After application, residues on food items are predicted to decline according to a first-order exponential model. If the maximum initial concentration is C_0 and the half-life for the exponential dissipation of the active ingredient is $t_{1/2}$, the remaining concentration at time t is given by the following formula:

$C_t = C_0 e^{-\frac{t \ln 2}{t_{1/2}}}$ or $C_t = C_0(1/2)^{t/t1/2}$ (the latter form shows the direct use of the half-life concept).

The general formula for the peak EEC (C_{peak}) following multiple applications is:

$C_{peak} = \sum_{i=1}^{n} C_0 e^{-\frac{I(n-i)\ln 2}{t_{1/2}}}$ or in simpler, directly calculable, single equation form,

$$C_{peak} = \frac{C_0[1-(1/2)^{nI/t1/2}]}{[1-(1/2)^{I/t1/2}]}$$

where C_0 is the maximum initial concentration after one application, I is the time interval between applications, n is the number of applications, and $t_{1/2}$ is the half-life of the active ingredient.

APPENDIX 4

Calculation of dietary concentrations (ppm) from Rat Acute Oral LD50 or Rabbit Developmental Toxicity studies in which gavage (mg/kg body weight) is used as the route of exposure.

Assessment of risk to small mammals when exposure is estimated as residues on food items requires that the daily dose values be converted to concentrations with units comparable to the residues units, ppm or mg/kg food wt, on mammal food items. An LC50 value in mg/kg food weight (ppm) is estimated from the LD50, and a residue in mg/kg food weight (ppm) is estimated from the daily dose in the rabbit developmental study for mammals having different diets as follows:

$$\text{1-day dietary residue(mg/kg food wt)} = \frac{\text{daily dose (mg/kg body wt)}}{\text{proportion body wt. eaten/day}}$$

Mammal Type	% body wt consumed per day	rat LD50 ____________________ _ rabbit developmental NOAEL (mg/kg body wt)	Estimated dietary equivalent mg/kg food wt (ppm)
Herbivore/Insectivore	66	823	1246
		12	18
Granivore	15	823	5486
		12	80

APPENDIX 5

Graphs of Maximum and Mean Crop Residues for all Use Patterns as a Function of Time, Showing Relationships to Reproductive and Developmental NOAELs

Discussion of Graphs (Figures 1-14). To characterize the possible impacts of longer term exposure, the following series of graphs shows the relationship of estimated dietary EECs over time and reproductive and developmental NOAELs from mammal studies. Note that the 'effect' in the developmental study was 100% mortality by day 29. Mortality to small mammals is possible from long-term dietary exposure. HED's review of the rabbit developmental study suggested that the data indicate even a single feeding might cause adverse effects.

The graphs depict all use patterns, and are given for both maximum residues and mean residues. Note that only insects and seeds are graphed, and green vegetation was not. This is because cacodylic acid/Na salt is a foliar desiccant, and it was assumed that foliage would dry up and die within a week. Thus the potential for long term exposure on green vegetation, as well as buildup from one application to the next, is considered to be low.

Figure 1. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in cotton fields treated 1 time at 1.2 lbs ai/acre and also showing mammalian chronic NOAELs. The registrant has proposed to reduce the use rate on cotton to 0.6 lb ai/acre.

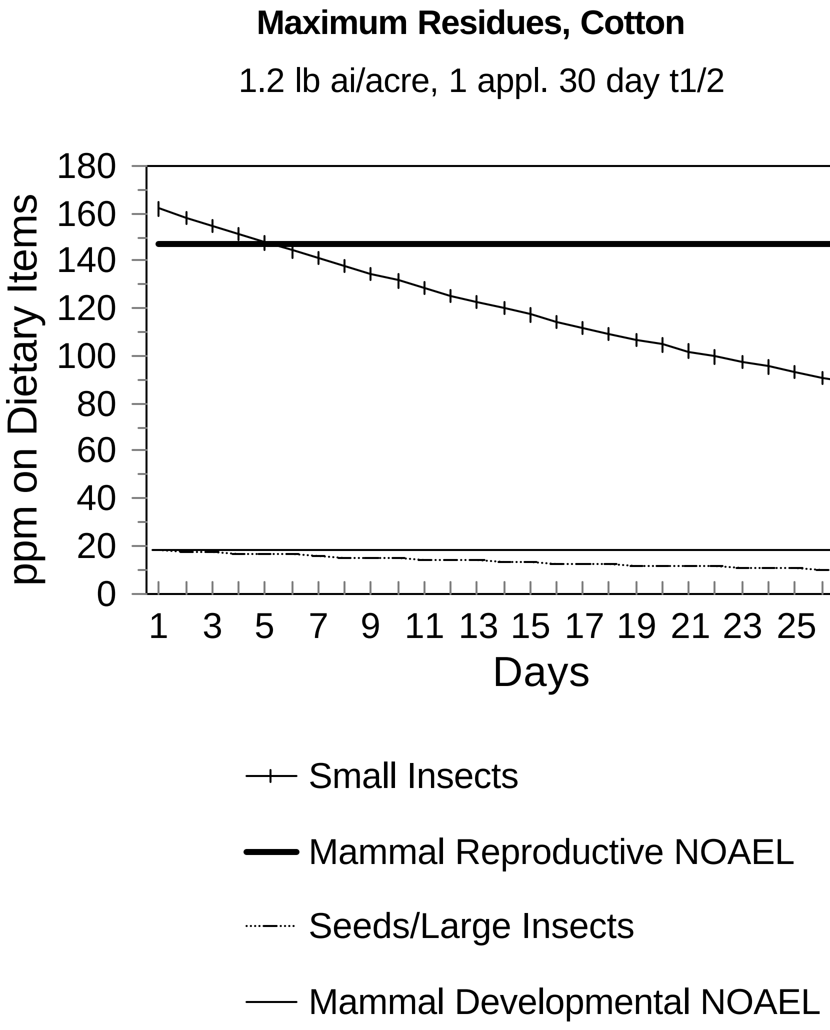


Figure 2. Graph showing *mean* long term cacodylic acid residues on seeds and insects in cotton fields treated 1 time at 1.2 lbs ai/acre and also showing mammalian chronic NOAELs. The registrant has proposed to reduce the use rate on cotton to 0.6 lb ai/acre.

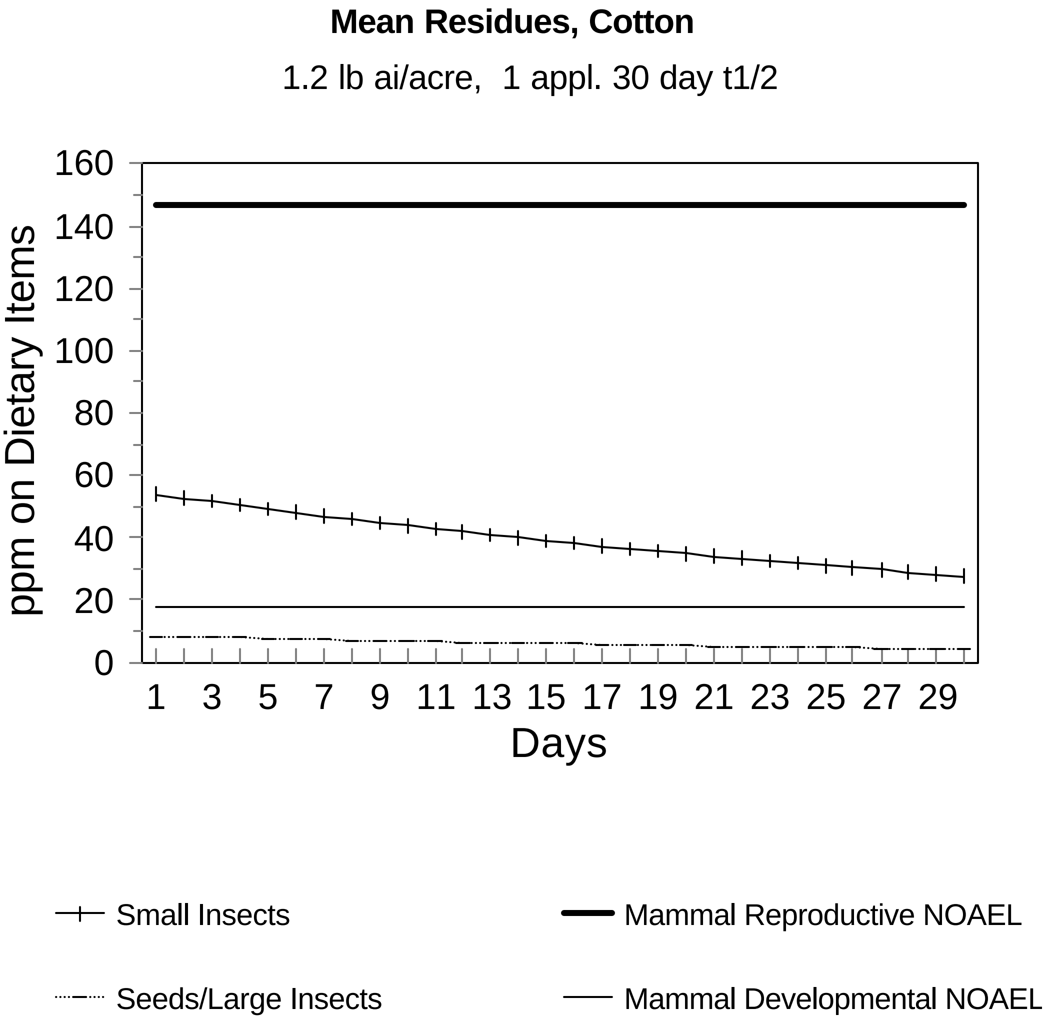


Figure 3. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in cotton fields treated 1 time at 0.6 lb ai/acre and also showing mammalian chronic NOAELs.

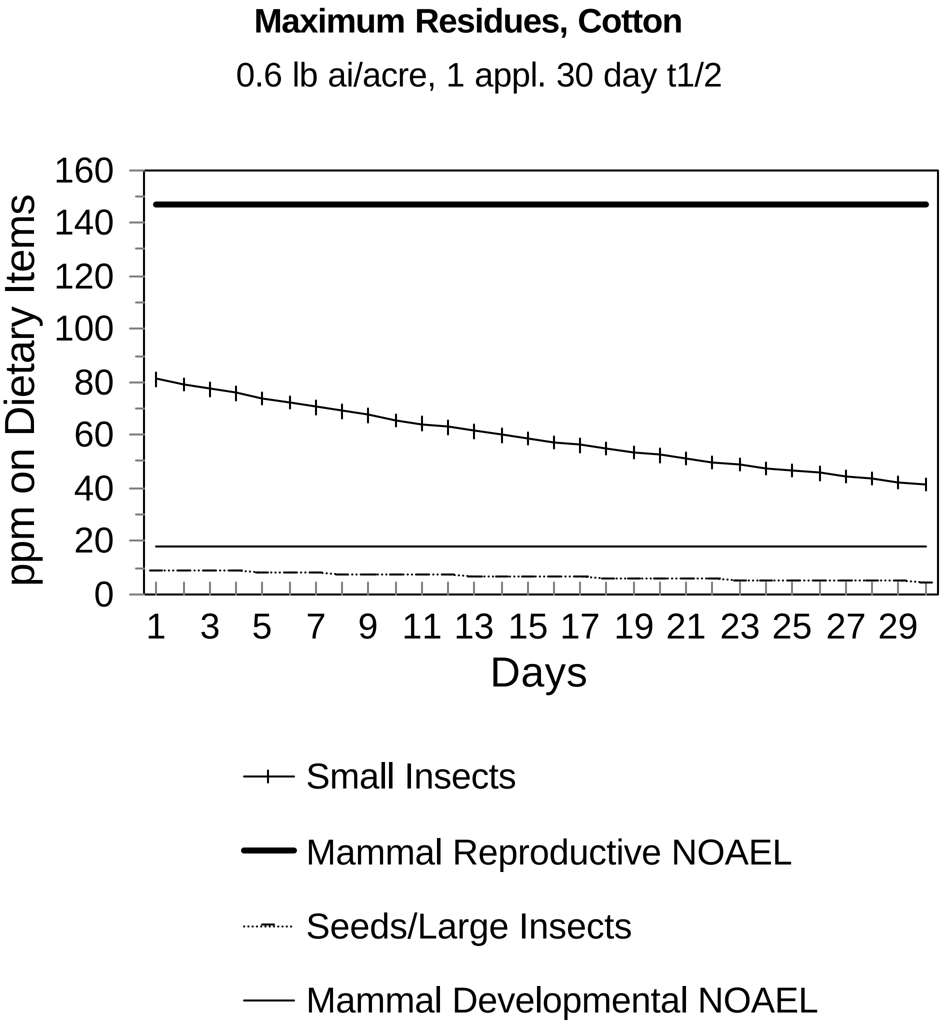


Figure 4. Graph showing *mean* long term cacodylic acid residues on seeds and insects in cotton fields treated 1 time at 0.6 lb ai/acre and also showing mammalian chronic NOAELs.

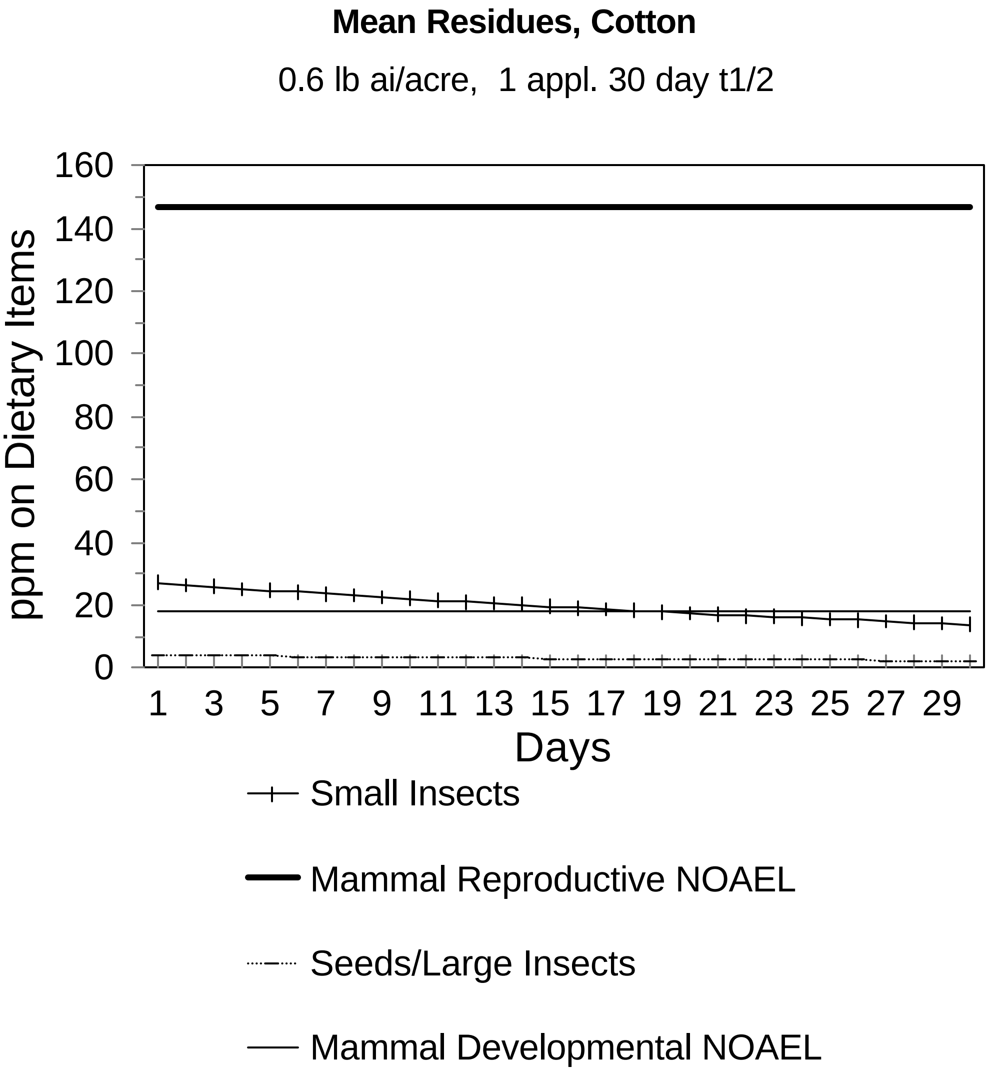


Figure 5. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in orchards treated 1 time at 5 lbs ai/acre and also showing mammalian chronic NOAELs.

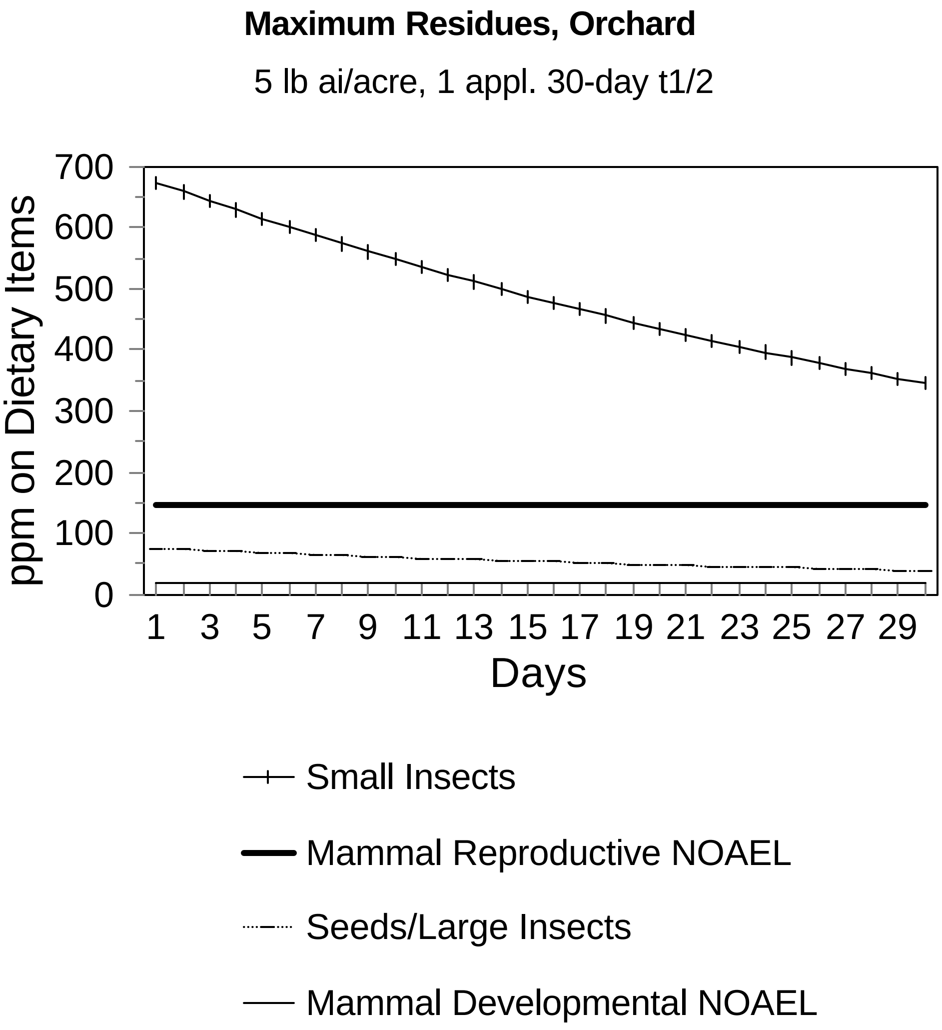


Figure 6. Graph showing *mean* long term cacodylic acid residues on seeds and insects in orchards treated 1 time at 5 lbs ai/acre and also showing mammalian chronic NOAELs.

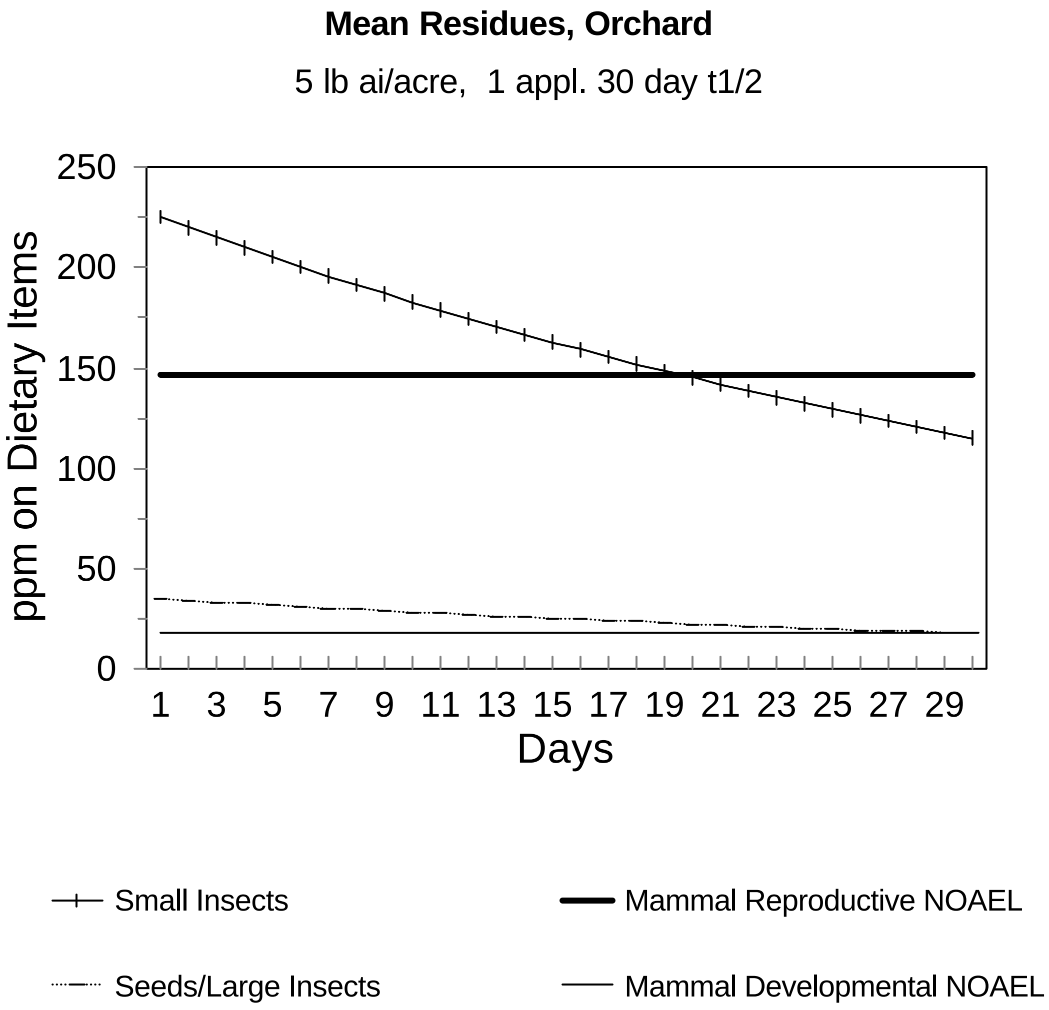


Figure 7. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in orchards treated 3 times at 5 lbs ai/acre and also showing mammalian chronic NOAELs.

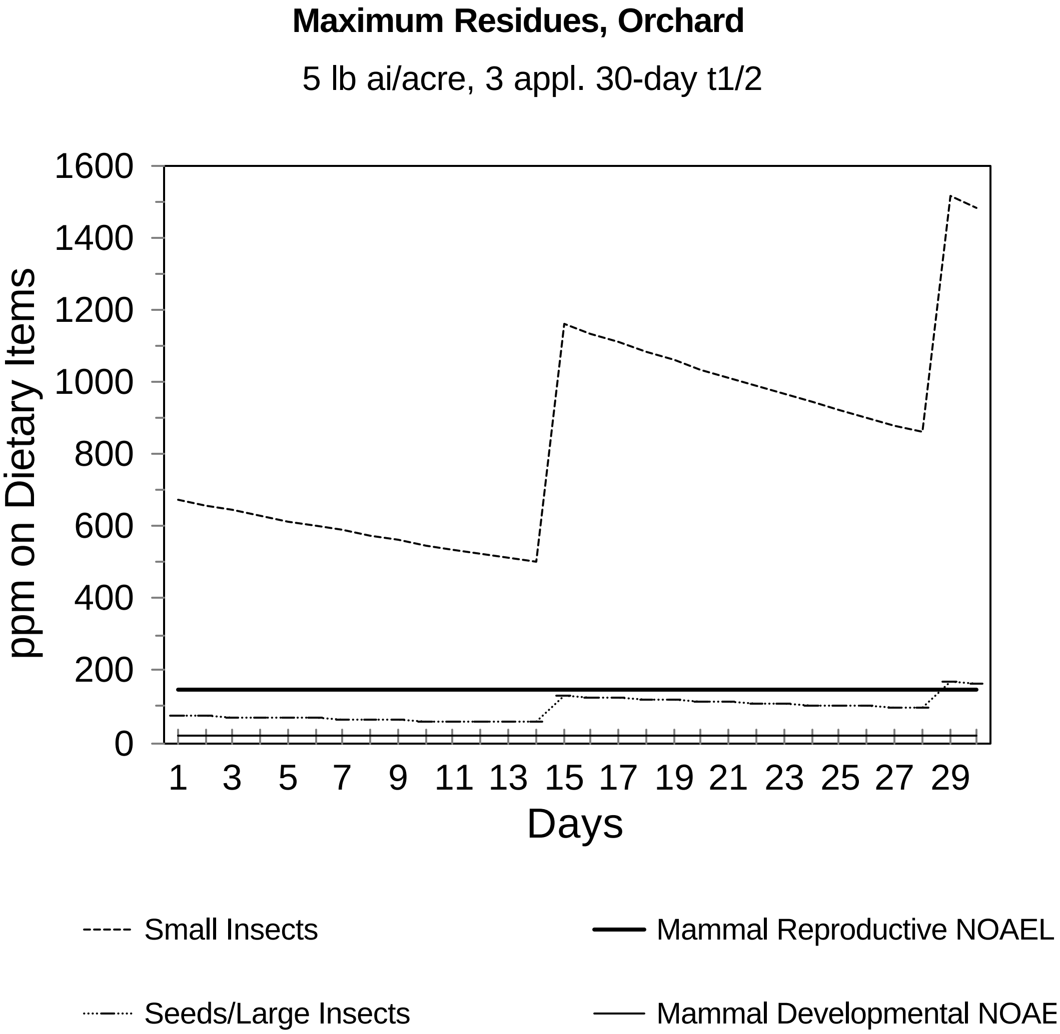


Figure 8. Graph showing *mean* long term cacodylic acid residues on seeds and insects in orchards treated 3 times at 5 lbs ai/acre and also showing mammalian chronic NOAELs.

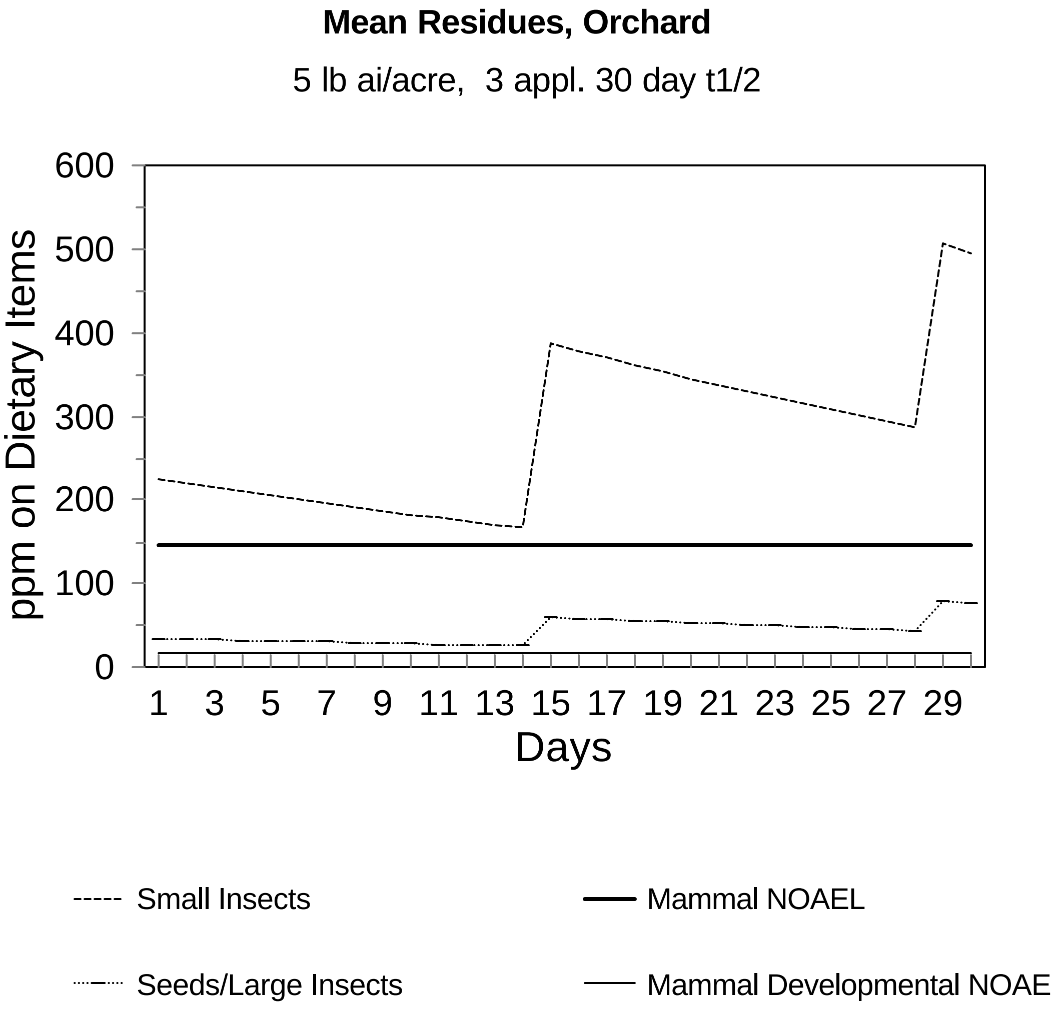


Figure 9. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in noncrop areas treated 3 times at 2.5 lbs ai/acre and also showing mammalian chronic NOAELs.

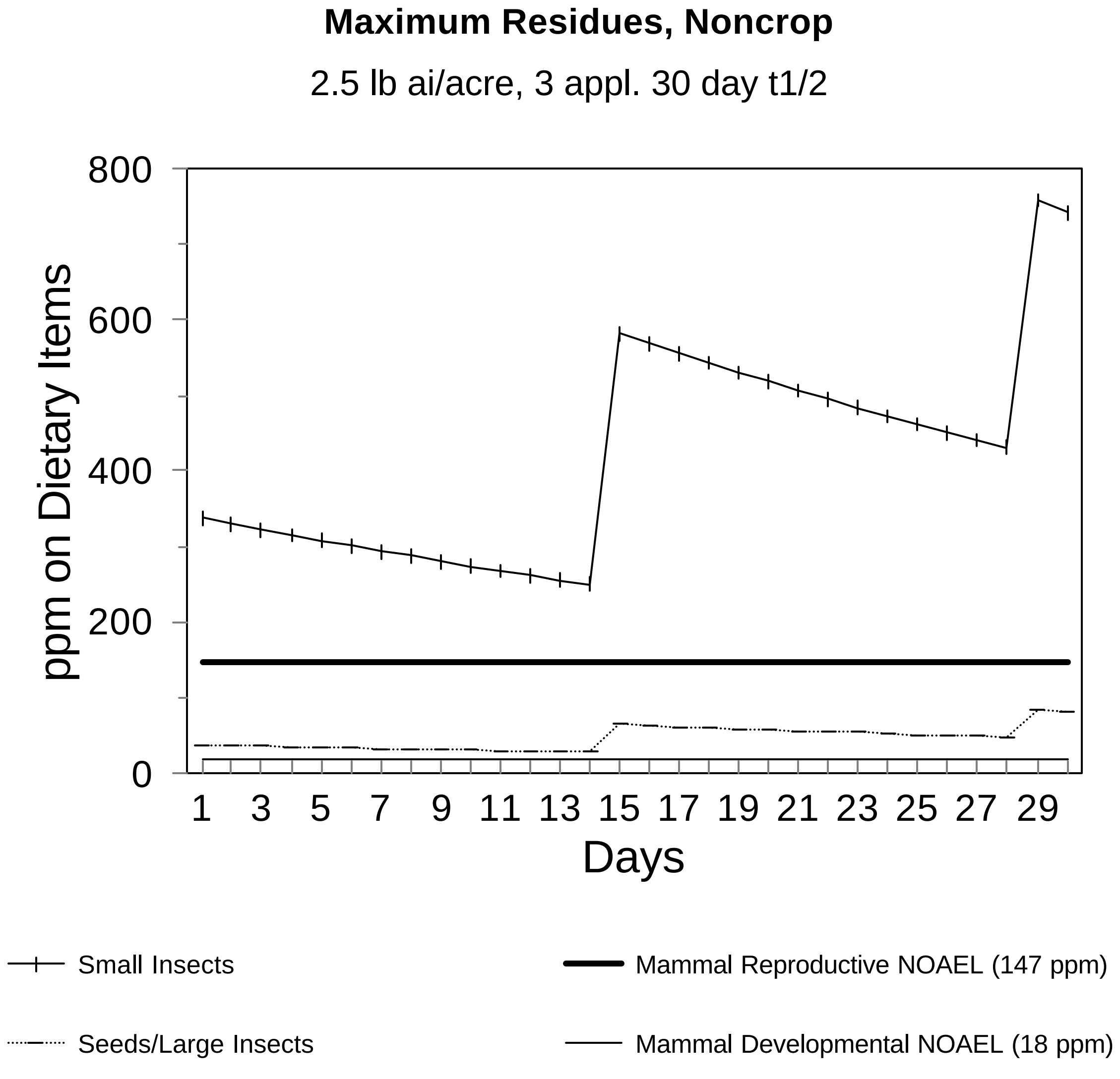


Figure 10. Graph showing *mean* long term cacodylic acid residues on seeds and insects in noncrop areas treated 3 times at 2.5 lbs ai/acre and also showing mammalian chronic NOAELs.

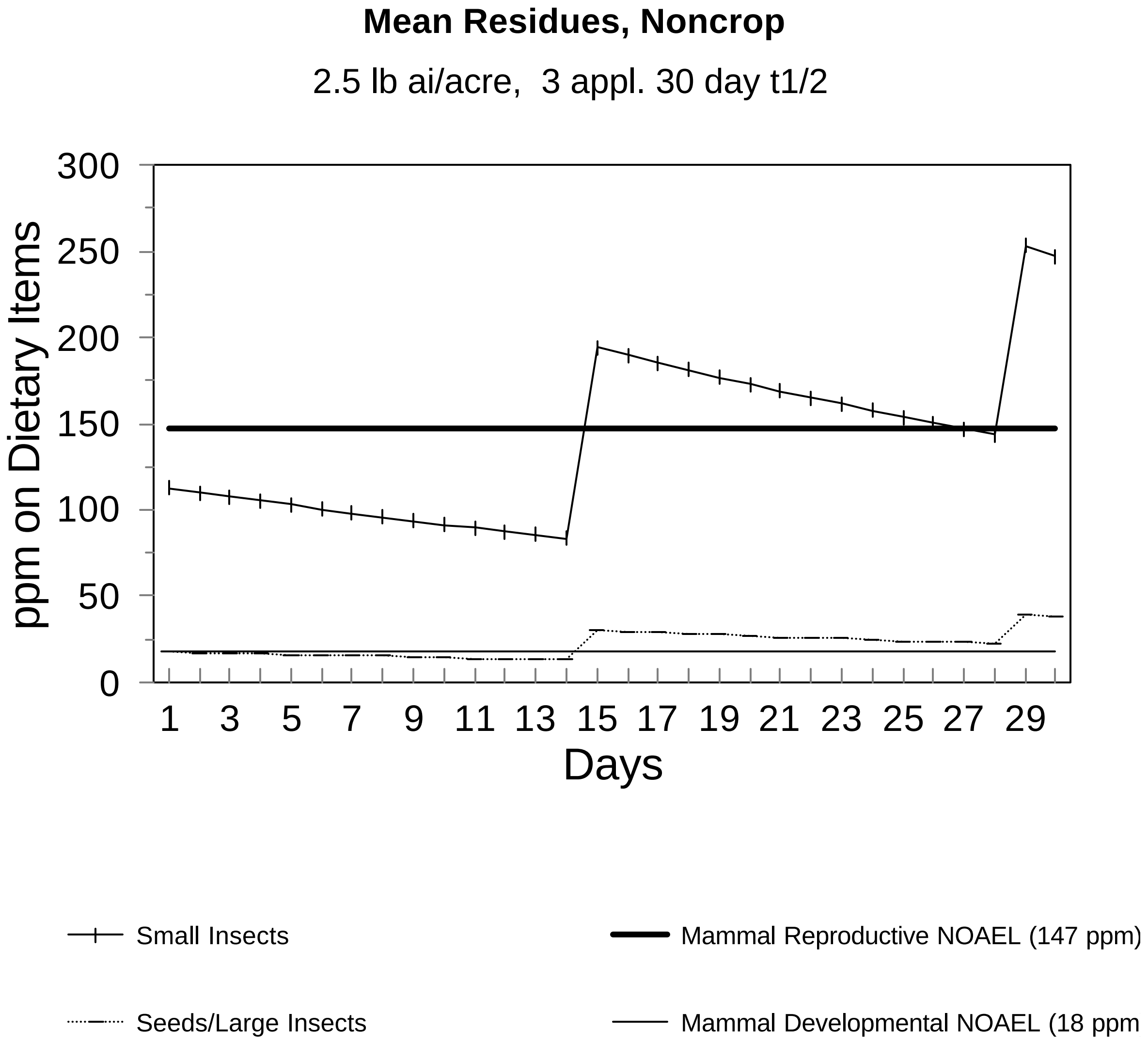


Figure 11. Graph showing *maximum* long term cacodylic acid residues on short grass, seeds and insects in noncrop areas treated 1 time at 8.1 lbs ai/acre and also showing mammalian chronic NOAELs. Short grass was added for this use pattern because it was assumed short grass might be abundant in noncrop areas.

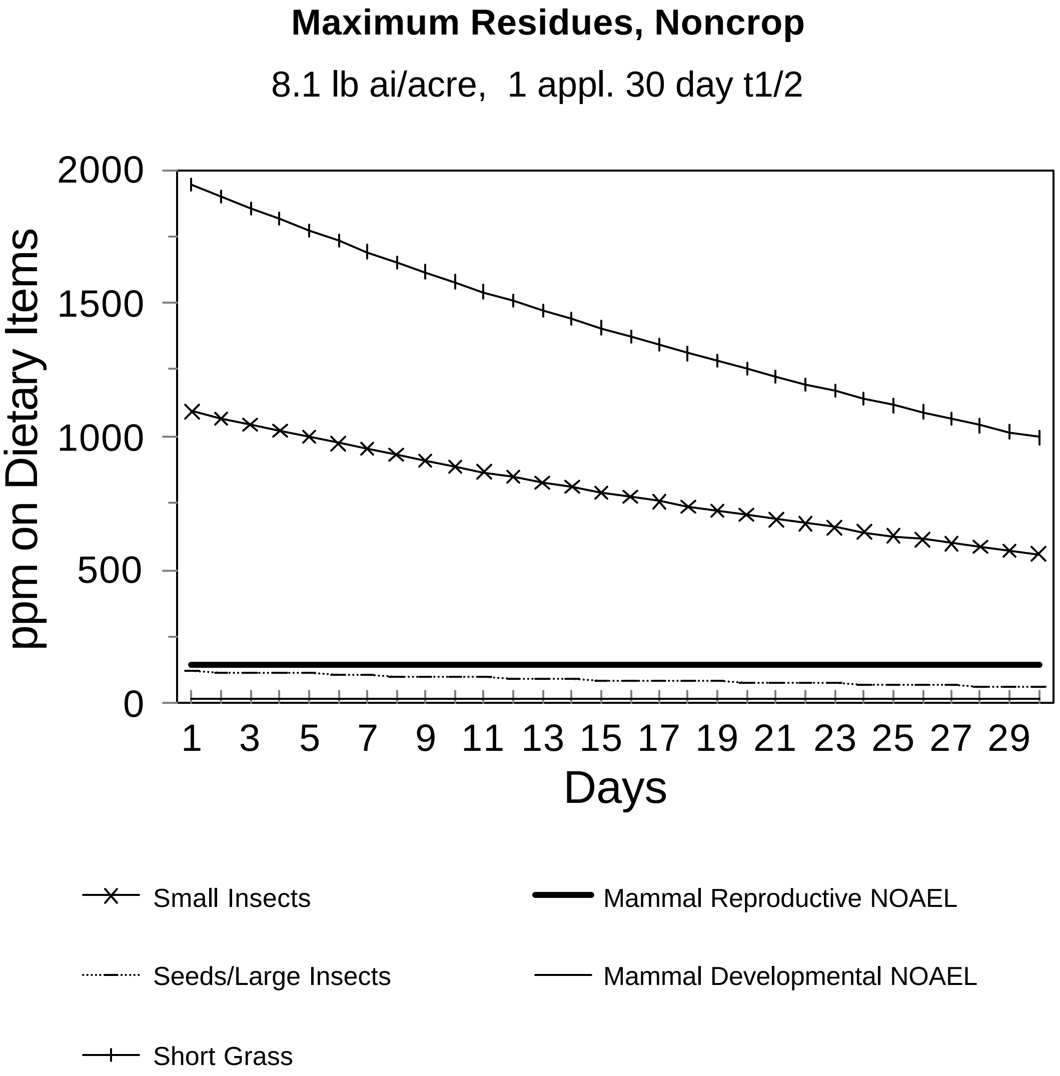


Figure 12. Graph showing *mean* long term cacodylic acid residues on short grass, seeds and insects in noncrop areas treated 1 time at 8.1 lbs ai/acre and also showing mammalian chronic NOAELs. Short grass was added for this use pattern because it was assumed short grass might be abundant in noncrop areas.

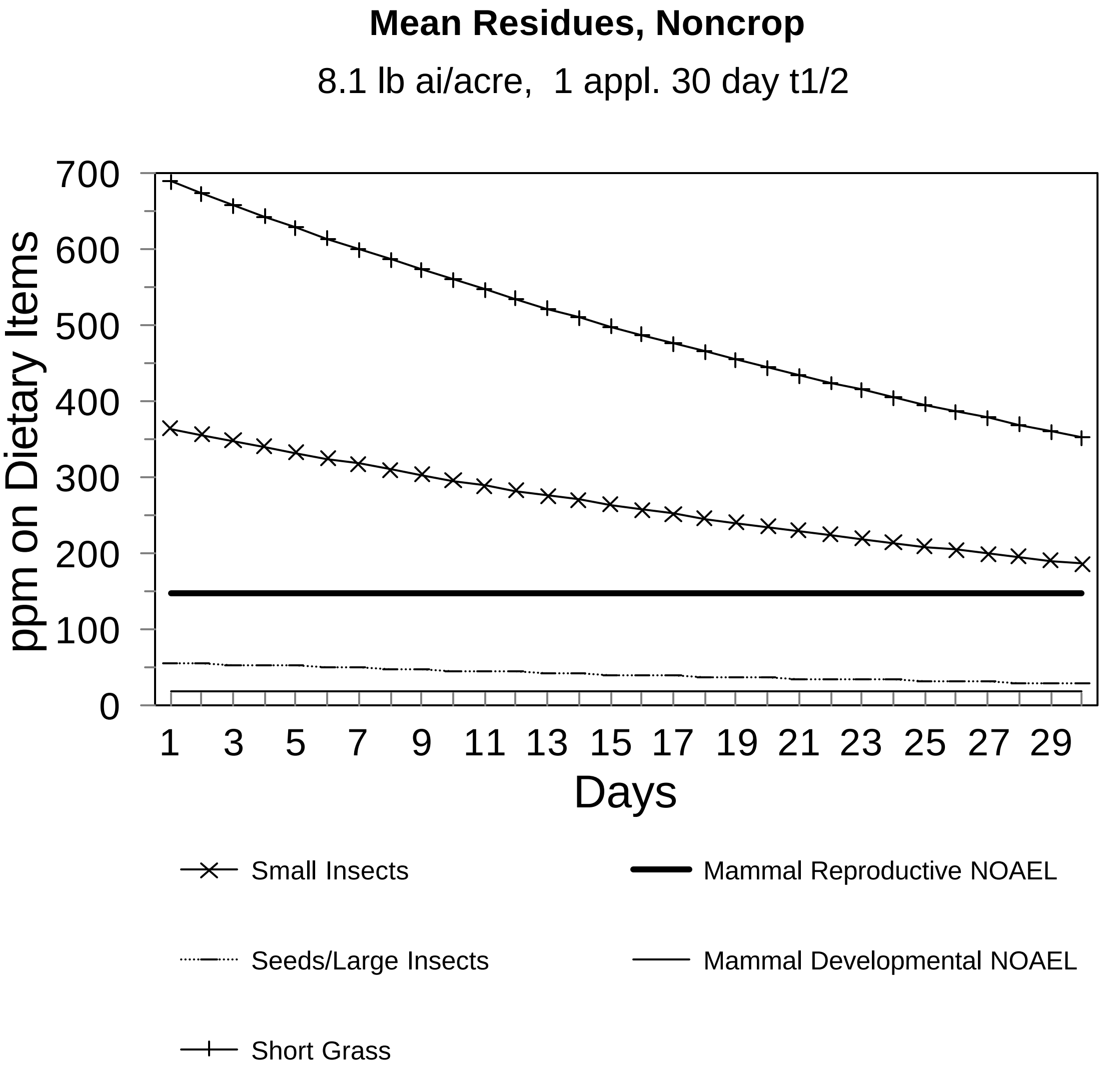


Figure 13. Graph showing *maximum* long term cacodylic acid residues on seeds and insects in noncrop areas treated 3 times at 8.1 lbs ai/acre and also showing mammalian chronic NOAELs. Short grass was not added for this use pattern even though short grass might be abundant in noncrop areas. It was assumed short grass exposed in the first treatment would dessicate and die, and therefore not be a food source on which residues would accumulate with multiple applications.

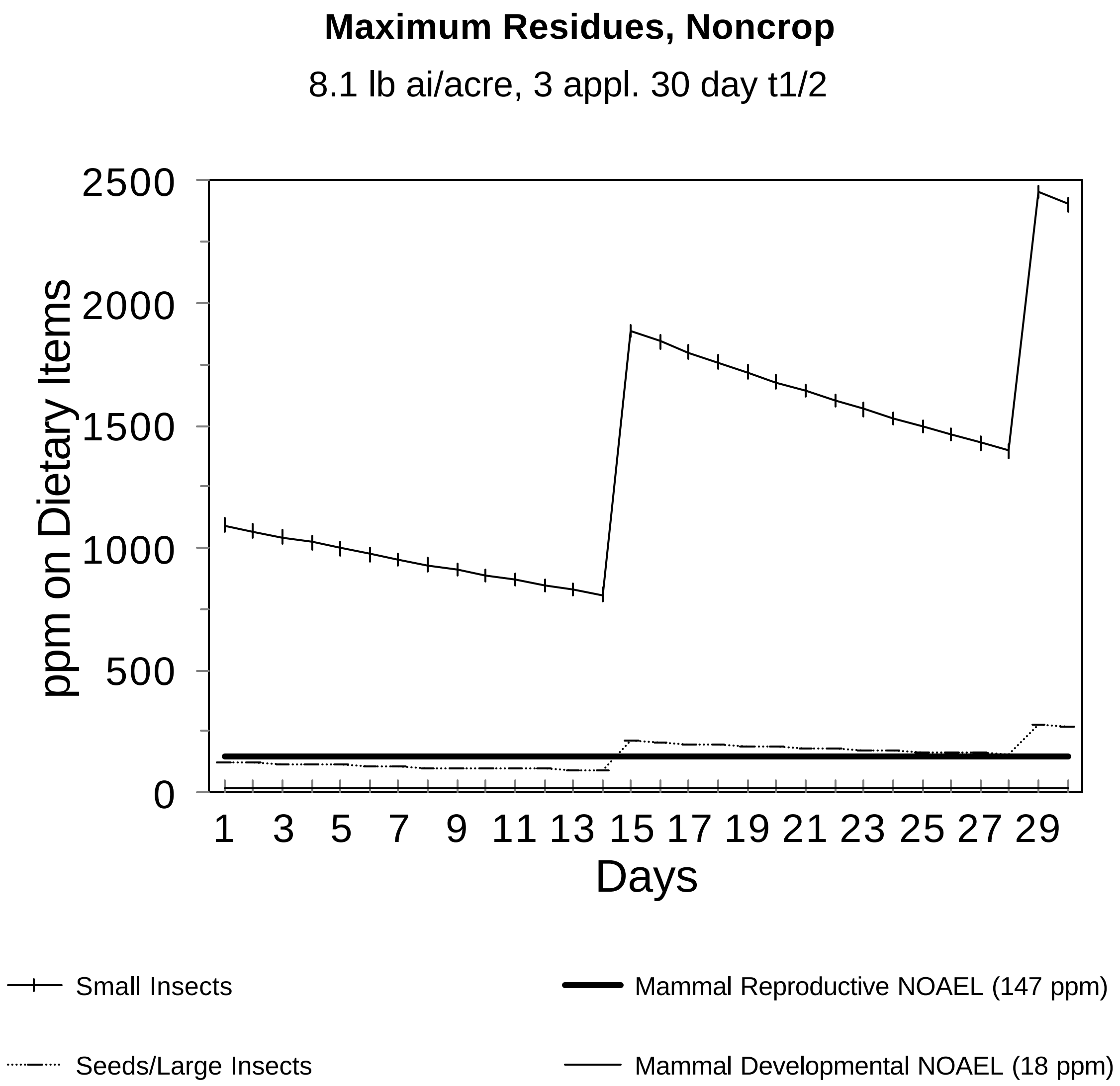
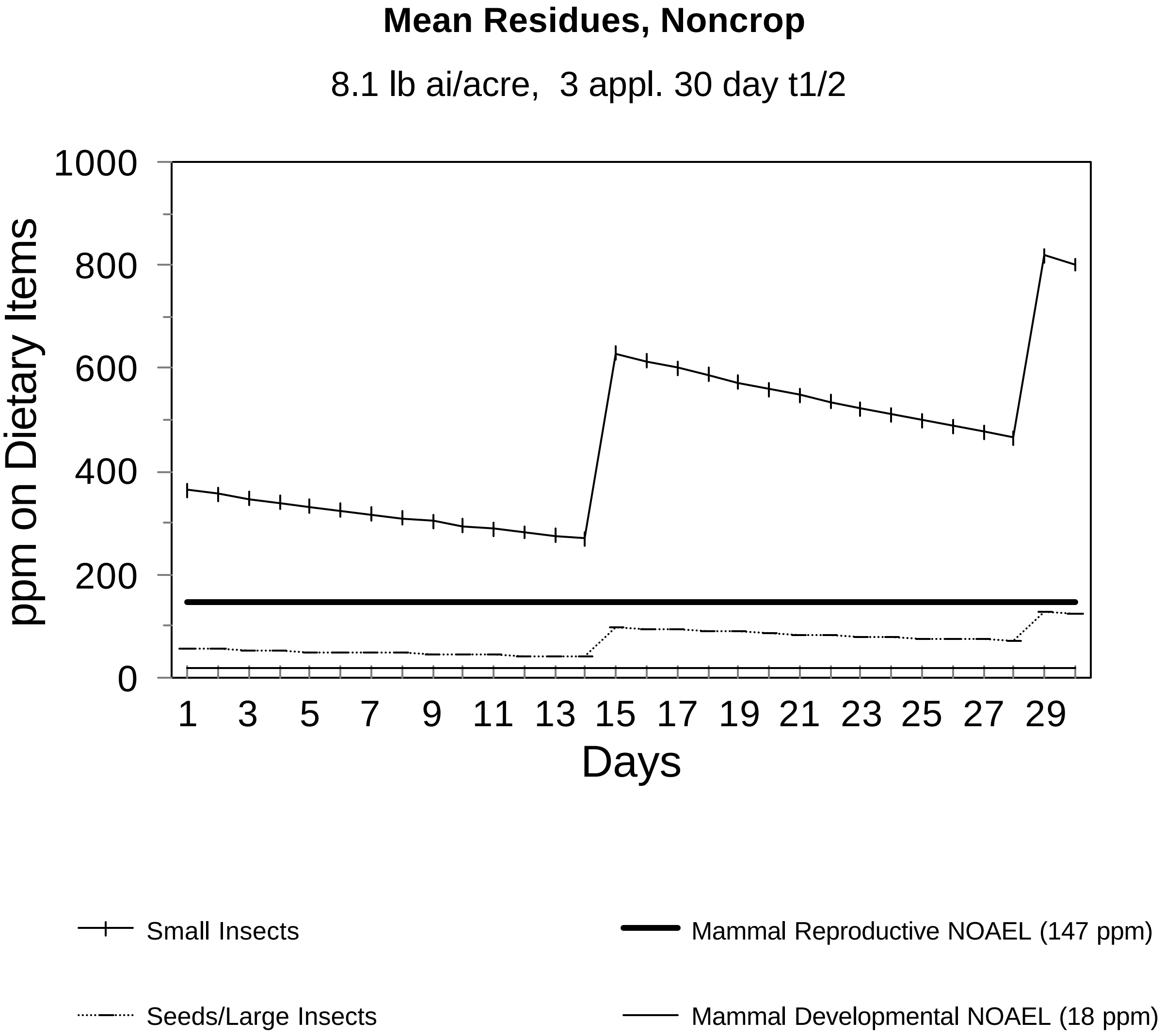


Figure 14. Graph showing *mean* long term cacodylic acid residues on seeds and insects in noncrop areas treated 3 times at 8.1 lbs ai/acre and also showing mammalian chronic NOAELs. Short grass was not added for this use pattern even though short grass might be abundant in noncrop areas. It was assumed short grass exposed in the first treatment would dessicate and die, and therefore not be a food source on which residues would accumulate with multiple applications.



APPENDIX 6

ENVIRONMENTAL FATE ASSESSMENT

(References are attached at the end of this Appendix. See Appendices 7 and 8 for co-joined model input and output parameters and chemical and physical properties. Chemical formulas and names are given in Appendix 9.)

Introduction and Basis

Cacodylic acid is one of several arsenic containing pesticides which the Agency is or soon will be considering for reregistration eligibility. Ultimately, in another action, the Agency will assess the potential overall (aggregate, cumulative) drinking water exposure to these compounds and common transformation products. The EPA Office of Water (OW) is scheduled to issue a proposed and final regulation on the larger issue of "arsenic" in drinking water by the years 2000 and 2001, respectively.

Because of historical toxicological interest in arsenic compounds (the name arsenic has been practically synonymous with "poison" for thousands of years), there is a substantial body of published and unpublished scientific study on their chemistry and environmental fate. Modern literature clearly shows that the biogeochemical interactions of these compounds are complex, and still the subject of active research. However, it is not within the scope of this document to comprehensively review this fascinating area. This has been done to a large extent in the past by the EPA in 1988, the National Academy of Sciences (NAS, 1977), the U.S. Department of the Interior's Fish and Wildlife Service (FWS, 1988), other agencies, individual scientists (e.g., ACS, 1975 Symposium), and very recently by the National Research Council (NRC, 1999; sponsored by EPA) and by the U.S. Geological Survey (USGS, see below). Although the focus here is on *cacodylic acid*, its place in the larger scheme should be understood at the outset.

Essentially all the arsenic since the earth's formation is still present and virtually immutable (barring nuclear transmutation), with new amounts added daily as cosmic dust. Soils, for example, commonly contain from 1-50 parts per million (ppm) of total arsenic, averaging around 5 ppm (Lindsey, 1979). Sediments average somewhat higher. Many of the compounds of arsenic, including our subject chemical, cacodylic acid, are synthetically manufactured (ultimately from some primary mineral source) and occur naturally and ubiquitously as well. All are subject to the same fate and transport processes, and are entwined inseparably as part of the global arsenic biogeochemical cycle. Cacodylic acid introduced locally through agriculture cannot be distinguished molecularly from that which is present in the natural background. Only unnaturally high localized concentrations would serve as a telltale. Likewise, other chemical forms of arsenic (organic or inorganic/mineral) resulting from the transformation of cacodylic acid or other arsenic sources which are either naturally present or introduced by human activities (e.g., other pesticides; fossil or wood fuels; agricultural burning; waste incineration; spreading of sewage sludge; poultry and swine manure; mining; smelting; congener contaminant in phosphate detergents and fertilizers; industrial production of semiconductors and glass) cannot, in general, be distinguished as originating exclusively from cacodylic acid. There is certainly much more arsenic in all environmental compartments (air, soil, sediments, water, plants, animals) than could ever be attributed to pesticidal application of cacodylic acid and other arsenicals.

Because of the established complexity, the environmental fate of cacodylic acid and other arsenicals cannot be adequately captured by standard FIFRA, 1988, Guideline studies, which are designed primarily for aspects of xenobiotic organic compounds subjected to a very limited set of experimental conditions. Therefore, in addition to the registrant's FIFRA studies performed under Good Laboratory Practices (GLP), the Agency relies substantially on the open scientific literature, including very recent publications (or some in press), for nuggets of information which directly impact the Office of Pesticide Programs (OPP) environmental fate and effects risk assessment for cacodylic acid. Even so, evidence is often highly variable or seemingly conflicting, indicating that processes, speciation, and environmental interactions (including effects of pH and oxidation-reduction conditions) among the various organic and inorganic species of arsenic are in constant biogeochemical flux and still incompletely understood.

Recent outbreaks of serious arsenic poisoning originating from drinking water wells in India and Bangladesh, as well as those long-established in Taiwan, have attracted the worldwide attention of newspapers and public health officials. Although these events are <u>not</u> associated with use of cacodylic acid, they have had the collateral effect of stimulating renewed scientific interest in the environmental chemistry and fate of arsenicals (Nickson, et al., 1998; Masud, 2000; numerous others). In addition, as will be discussed under the drinking water exposure assessment section of this document, recently completed projects by the USGS and the pending regulation by the EPA Office of Water also attest to the interest in arsenicals in our environment. A better understanding of the many facets of the environmental chemistry and potential risks of environmental arsenic is evolving.

Assessment

<u>Degradation/Metabolism.</u> The Agency is presented with two opposing alternatives: the first results from those studies which the registrant submitted under FIFRA and GLP; the second, from published studies which registrant submitted prior to FIFRA and from numerous other studies published up to the present day in the open scientific literature.

All environmental fate laboratory studies submitted under current Guidelines (FIFRA, 1988) and Good Laboratory Practices (GLP) criteria ("new studies") showed that cacodylic acid was stable under all tested conditions. That is, cacodylic acid did not degrade under the influence of chemical, photochemical, or aerobic and anaerobic microbial metabolic processes in soil or water (study summaries and citations attached). Thus, on the basis of submitted GLP laboratory results, cacodylic acid would be expected to accumulate indefinitely in the environment at concentrations commensurate with its usage and physical dispersal or transport processes. This is a surprising outcome because:

1) numerous publications in the open technical literature, including those which the registrant submitted for the purpose of registration prior to FIFRA, 1988 and GLP, as well as some very recent publications, show significant laboratory and field soil metabolism;

and

2) cacodylic acid, a component of the earth's natural arsenic cycle[1], has not noticeably accumulated on the planet;

The apparent persistence of cacodylic acid in the GLP studies could therefore be an artifact of experimental conditions or unique and undetermined experimental media characteristics (such as media sterility). Some of the possibilities are discussed below.

The published studies, as discussed further below, show widely differing rates of soil metabolism which depend strongly on soil moisture, temperature, organic matter, and pesticide concentration (half-lives from around 20 days to several years). Other factors such as pH, redox potential, and other soil properties are most likely important, but EFED is not aware of systematic investigations on the effects of these on cacodylic acid reactivity.

Supplemental and inconclusive GLP terrestrial field dissipation studies, although suffering from important deficiencies, add inferential information on stability and environmental fate. Noteworthy deficiencies in these field studies were: 1) there was failure to account for apparent loss or "disappearance" of parent cacodylic acid by not demonstrating routes and products of transformation; 2) there was net loss of total applied arsenic (roughly 20 to 60% in approximately one year of immutable arsenic), apparently without leaching; 3) there was no sampling for potentially volatile products to account for losses, and 4) inorganic forms of arsenic were not speciated. Minor amounts of methane arsonate (equivalent to MSMA), possibly artifacts of chemical procedures, were detected, indicating little production of MSMA or very transient existence. Since from other studies MSMA is known to have an extended environmental lifetime, MSMA is, therefore, not formed as a major metabolite. [Other studies (discussed below) support the virtually simultaneous loss of two methyl groups from cacodylic acid, rather than a slower sequential change through a longer-lived MSMA by loss of a single methyl.] The most recent field study submission (duplicate MRIDs of 42843101 and 43485301 for a 1993 study) ostensibly shows a "disappearance" of cacodylic acid which corresponds to a half-life of approximately 22 days. This, of course, is contrary to the stability expected from the results of the GLP lab studies. The inference from the loss of arsenic, since leaching was not significant, is that some other form(s) of offsite transport, perhaps untested loss of volatile arsenic species, are

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[1] As part of the arsenic cycle, cacodylic acid is a methylated by-product resulting from, among other things, normal dietary ingestion and metabolism of various arsenic compounds found naturally in food and water. Humans, for example, as an integral part of the global arsenic cycle, convert (primarily in the kidney and liver) much or most of the organic and inorganic arsenicals ingested from natural foods into cacodylic acid which we excrete in our urine (there is extensive literature on this subject).

operational. Since parent is not volatile, any loss as volatile products also implies chemical or biochemical transformation, contrary to the laboratory reports of stability. Thus, the registrant, through FIFRA GLP studies, presents an unresolved environmental fate profile for cacodylic acid.

Contrasting with the "new" GLP lab studies, and more consistent with the global picture of the absence of vast accumulations of cacodylic acid and the inference from field study results, are laboratory studies submitted in support of registration prior to establishment of the current, formal Guidelines and GLP criteria, and other studies published in the open technical literature (some very recently, see below). [The registrant submitted the prior studies under Accession Nos. 259582, 260061, 260782 (Agency review 27 June 1986).] These studies clearly show soil microbial metabolism to be a major route of transformation which produces variable proportions of inorganic arsenicals, carbon dioxide, and volatile organic arsenicals. Estimated first-order half-lives in aerobic soil have ranged variously from around 20 days to several years, depending in a complex way on soil characteristics and ambient conditions such as soil moisture, temperature, and organic matter. Adding to the complexity is that metabolism rates sometimes did not depend linearly on cacodylic acid concentration, but decreased with increasing concentration. Hence, the kinetics are not necessarily first-order, and "half-life" is therefore not necessarily a convenient constant for all concentrations. One possible reason for the slowing of metabolism at increasing concentrations could be toxicity to soil microorganisms. However, within the range of labeled application rates, this effect is minimal compared to other factors, as discussed later in this document.

The aerobic and anaerobic soil metabolism discussion in the 27 June 1986 review (Accession Nos. above) was based on a published laboratory study by Woolson and Kearney (Woolson, 1973) in which the authors used ^{14}C-cacodylic acid at three concentrations (1, 10 and 100 ppm) in each of three soils of varying iron and aluminum content. Soil moistures were brought to 75% of field capacity and the temperature was 25 ^{0}C. For several reasons (discussed in this document as an expanded part of the Appendix 10 Study Summaries), this study certainly does not meet current guideline standards, but was not specifically cited as deficient in the 1986 Agency review, and provides valuable information. Results of the present reregistration reevaluation of the metabolism data from this published study, although somewhat subjective, yield assumed first-order aerobic half-lives for the three soils of 16.7, 12.7, and 6.9 weeks after 24 weeks of incubation. With less data (fewer replicates) for anaerobic (flooded) soil metabolism, apparent half-lives were 12.3, 19.7, and 22.7 weeks after 24 weeks of incubation. Again, these estimated results are dependent on professional judgment and interpretation. The nature of transformation products revealed in this and other studies is integrated below in the "metabolites" subsection.

Other published studies submitted under the same Accession Numbers for the 1986 Agency review (some by the same authors), but apparently not specifically evaluated at that time, yielded other half-lives under a variety of conditions. Woolson et al (Woolson, 1982) reported the residual cacodylic acid to average approximately 15-30% of the initial concentration of approximately 18 ppm (10 ppm arsenic) after 60 days of aerobic incubation at 25 ^{0}C in a Mattapeake silt loam soil treated under several different conditions of soil moisture (77-230% of field capacity) with unamended soil and with a variety soil amendments (equivalent to 50-100 tons/ha). Results were similar under all conditions. Based on these published data the registrant correctly estimated an average aerobic soil half-life (assumed first-order) for all amended treatments to be approximately 31 days. The estimated half-life from unamended soil was approximately 20 days.

In like manner, based on yet another Woolson paper (Woolson, 1977) with the same initial cacodylic acid concentration of approximately 18 ppm (10 ppm arsenic) with the same Mattapeake soil amended with about 6% ground soybean meal and with a soil moisture content of only 25-30% of field capacity, the registrant correctly calculated an extrapolated aerobic soil half-life (based on 82% of cacodylic acid remaining after 160 days of aerobic incubation) to be roughly 1.5 years (559 days). In the same study, the analogous, extrapolated anaerobic soil half-life (based on approximately 92% remaining after 160 days at the same soil moisture content, but with a nitrogen atmosphere), would be roughly 4 years. The higher organic matter and low moisture conditions would not be typical of most agriculture.

Again, none of these published studies meet current Guideline and GLP criteria. For example, half-life estimates were generally based on single time intervals, rather than a series of time intervals; there was generally limited, non-systematic or inferred identification of metabolites; and direct accounting for radioactivity in all compartments (material balance) was either not attempted or low. However, these studies appeared formally in peer-reviewed scientific publications, as is normal for most scientific work outside of the regulatory process; have been cited in the literature numerous times, including by the NAS, NRC, and the FWS; and were submitted by the registrant in the past. These studies provide a body of evidence on the environmental fate of cacodylic acid that cannot be dismissed.

More recently, Gao and Burau (Gao, 1997) have published an excellent study systematically designed to measure the influence of four factors--concentration, soil moisture, temperature, and soil amendment with organic carbon (cellulose)--on the rates and routes of transformation of arsenicals in soil. For this purpose, they tested four arsenicals: 1) sodium arsenate [As(V)]; 2) sodium arsenite [As(III)]; 3) (mono)methanearsonic acid; and 4) our subject chemical, cacodylic acid, in the form of sodium cacodylate. The study was, however, limited to one California soil, a Sacramento silty clay (noncalcareous). Of the four compounds, the authors treated cacodylate far more extensively. In their report, Gao and Burau also provide an excellent, introductory review and bibliography of previous work on the subject of arsenicals in soil. In this respect, their coverage is more comprehensive than that given in this reregistration document, and would be valuable to those with particular interest in the subject.

Gao and Burau were motivated by noticing differences in published results on transformation processes (rates and products), especially in the proportions of volatile arsines evolved, and by a concern for the potential for arsenic to accumulate in soils. Accumulation is a concern because of increasing toxicity to plants and wildlife, and the possibility of migration of arsenic species to water resources. Many published studies of cacodylic acid and other organic arsenicals report production of major amounts of inorganic (mineral) arsenate and the evolution of volatile arsines (chiefly di- and tri-methylarsine). The loss of arsines to the atmosphere reduces localized build up of arsenic species and could be a main avenue of global arsenic redistribution. However, in other studies, transformation to volatile arsines was much lower. Thus, the extent to which an applied arsenical and its arsenic containing byproducts accumulates locally depends on both mineralization and volatilization. The 1997 Gao and Burau study serves to systematically complement, and, to a great extent, unify existing data. It also reveals the inherent limitations of the regulatory standard Guideline study for characterizing metabolism in soil.

Gao and Burau's results show the great influence of soil environmental conditions on transformation rates. After 70 days of aerobic incubation, depending on conditions (described below), the percentage of cacodylate mineralized to arsenate ranged from a low of about 3% (97% remaining) to a high of about 87% (13% remaining). Arsenite was not a detected product under these conditions. Using a first-order approximation for this single time interval, corresponding Agency calculated "half-lives" would range from approximately five years to approximately 24 days, respectively (see below). Mineralization observed after the 70-day incubation period depended strongly on all four tested factors:

1) Soil Moisture. At five soil moisture contents of 50, 250, 350, 450, and 550 g water/kg soil [from approximately 7% (-23.7 MPa suction) to 81% (-0.0005 MPa) of saturation], at 22 ^{o}C, and at an arsenic equivalent concentration of 100 mg/kg soil, mineralization to arsenate increased with soil moisture from the stated 2.7% to 86.6%. The Agency calculates decreasing apparent half-lives, respectively, of approximately 4.9 years, 2.0 years, 1.0 years, 67 days, and 24 days, showing the tremendous influence of soil water.

2) Temperature. At 5 and 25 ^{o}C [with cacodylate at the arsenic equivalent of 100 mg/kg soil and at a soil moisture content of approximately 1/3-bar suction (-0.03 Mpa)], mineralization was approximately 5.3 and 23.9%, respectively, which would correspond to first-order half-lives of about 2.5 years and 180 days, respectively. This result is roughly as would be predicted from the Arrhenius relationship which yields rate doubling for every 10 ^{o}C increase in temperature. [The 180 day (0.5 year) result can be compared with the 1.0 year soil moisture result above as a measure of variability under essentially the same conditions, except for an uncorrected 3 ^{o}C difference in temperature.]

3) Concentration. At *increasing* cacodylate concentrations equivalent to arsenic concentrations of 10, 30, and 100 mg/kg soil [(at 25 ^{o}C, and at a soil moisture content of approximately 1/3-bar suction (-0.03 Mpa)], *decreasing* percentages of cacodylate mineralized were approximately 82, 31 and 24%, respectively. Simple Agency computation of apparent "half-lives" from these results yields widely varying "half-lives" of approximately 28, 130, and 177 days, respectively, clearly indicating the rate process is not first-order in concentration[2]. One possible reason for the slowing of metabolism at

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[2] Gao and Burau did not compute apparent half-lives from these single time interval data, but state that the rate process is first-order with concentration based on inspection of a plot some of their data at the three test concentrations (their Fig. 6). At first inspection, the plot seems to give a reasonably linear result with applied concentration. However, it is the *change* in

increasing concentrations could be toxicity to soil microorganisms. However, the two upper concentrations correspond to application rates much higher than those currently labeled (maximum labeled, annual application rates correspond to a soil concentration roughly equivalent to 12 mg/kg of cacodylic acid or 6 mg/kg of arsenic).

4) Organic Matter. *Increasing* cellulose additions of 0.0 (unamended), 0.2, 1.0, and 5.0 g per 100 g of soil (original soil organic carbon content of 1.8%) with sodium cacodylate added at the arsenic equivalent of 10 mg/kg soil, at 25 ^{0}C, and approximately 1/3-bar soil suction (-0.03 Mpa)] *decreased* mineralization from around 77% down to around 49%. The results correspond to Agency calculated apparent half-lives of approximately 33, 35, 63, and 71 days. (As a measure of variability in this experiment under the same conditions, the first value of 33 days can be compared directly with the 28 day result from the concentration experiment above.) Some reports show the same trend of decreasing mineralization with increasing concentration of organic matter (e.g., Woolson, 1982), but others report the opposite trend (e.g., Dickens and Hiltbold, 1967). Types of added organic matter were generally different, and could perhaps account for the differences. However, in view of the sensitivity of metabolism to the other cited factors, lack of extremely careful control of experimental conditions could also be a major factor for the difference.

Using the Gao and Burau data to estimate an “effective” or more relevant environmental “half-life” (realizing that the process is apparently not first-order with concentration), the Agency interpolated the metabolism rate data cited above as a function of soil moisture at the tested arsenic equivalent concentration of 100 mg/kg soil to the standard 75% of 1/3-bar soil moisture content using the soil moisture retention function (the logarithm of the absolute value of soil tension vs. soil water concentration) which the authors gave for the Sacramento silty clay soil. The interpolation gives a moisture concentration of approximately 27% or 266 g water per kilogram of dry soil, and a corresponding half-life of 642 days (1.8 years). In tandem, the Agency then made a simple, proportionate adjustment of the rate constant corresponding to this half-life at the 100 mg/kg concentration to the more agriculturally relevant 10 mg/kg arsenic equivalent (18 mg/kg cacodylic acid). (Labeled application rates correspond to a soil concentration range of approximately 0.3 to 12 ppm with soil incorporation to a depth of 15 cm. This range is relatively low when compared to most study concentrations which were typically 10 to 180 ppm in cacodylic acid). This procedure results in a normalized half-life (at 75% of 1/3-bar soil moisture and an arsenic equivalent concentration of 10 mg/kg of 102 days.

Averaging this 102 day result derived from Gao and Burau’s 1997 publication with the aerobic soil half-life results for the three soils which Woolson and Kearney studied under standard conditions in 1973 (117, 89, and 48 days after 24 weeks of incubation), and with the standard results derived from

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concentration with time, not the concentration at a given time, that should be plotted versus concentration. Had they estimated half-lives they would have realized the discrepancy, and that the apparent linearity was coincidental. A differential plot shows the process is not first-order.

the unamended single soil in the 1982 Woolson et al. study (20 days after 60 days of incubation), yields an "effective" or "normalized" mean half-life (under standard conditions of 75% of 1/3 bar soil suction, a temperature of 25 ^{0}C, and for concentrations of cacodylic acid at the upper end of labeled application rates) of 75 ± 40 days with a standard upper 90% confidence limit on the mean of 103 days (3.4 months). (Because of the atypical conditions of the 1977 Woolson study, the Agency is not using its results for averaging.) The derived average of 75 days result stands in opposition to the indeterminately long or "infinite" results from the GLP lab studies.

Why the FIFRA GLP lab results which show cacodylic acid to be stable against metabolism in aerobic soil (only one soil tested) and in aerobic and anaerobic water/soil-sediment systems (one aerobic aquatic soil system and one anaerobic aquatic sediment system tested) are in stark contrast to all other reported observations (including the absence of accumulating quantities on the planet) is unclear. Failure to correctly determine and maintain adequate soil moisture, lack of microbial viability (system sterility), or other peculiar or unique features in the GLP studies could account for the opposing results. However, the registrant did not systematically test these and other possible experimental factors in an effort to explain the puzzling difference. A general and serious impediment for comparing results from all studies from all authors was the absence of a good measure of system biological activity which could have been determined by soil respiration or through use of benchmark compounds.

Metabolites. It is clear from the published literature that mineral arsenate (AsO_4^{3-}, which is ubiquitous in soil) and carbon dioxide are primary aerobic soil metabolites which result from microbial demethylation of parent cacodylic acid. Volatile organo-arsenic compounds (arsine or methylated arsines, see below) were produced in widely varying proportions in different studies or under different study conditions, and ranged from less than a fraction of a percent of applied cacodylic acid in some cases (Gau and Burau, 1997), to as high as around 60% in others (Woolson, 1973). However, the exact identities of these compounds were either not individually resolved by the analytical methodologies or inferred indirectly by difference from total remaining arsenic and qualitative measures such as distinctive odor. Dimethylarsine and possibly trimethylarsine were the consensus as being the most likely among several volatile candidates. According to Braman (ACS, 1975, chapter 8), these two compounds were actually identified in significant amounts as they were evolved on turf. Likewise, Woolson (Woolson, 1977) identified these two compounds (methylarsine was absent) in laboratory soil under both aerobic and anaerobic conditions.

Noteworthy is that the "obvious" candidate, the non-volatile solid methanearsonic acid [also designated as methanearsonate or as its equivalent salt monosodium methanearsonate (the herbicide MSMA)], if detected, was only a very minor product in lab or field soil. Coupled with prior knowledge from other studies of the relative stability of MSMA, this latter result clearly suggests that cacodylic acid degrades to arsenate primarily by virtually simultaneous loss of both methyl groups, rather than stepwise by going through the intermediate MSMA stage with the loss of one methyl and then subsequently to mineral arsenate by loss of the second methyl. In the one available aerobic soil laboratory study where there was analysis for the mineral transformation product arsenite (AsO_3^{3-}) (Gau and Burau, 1997), it was not detected. Consistent with this result and as part of the same study, applied arsenite was converted to arsenate. It is generally accepted and consistent thermodynamically that arsenate rather than arsenite is the prevalent form in aerobic soils. There were no reported tests for arsenite production from cacodylic acid under anaerobic or flooded conditions. However, comparable concentrations of arsenate and arsenite can thermodynamically coexist under certain environmental conditions, including those found in groundwater and surface water; and, indeed, such concentrations have been measured, as will be discussed elsewhere in this document. Ultimate arsenic balance is governed by the summation of shifting proportions of mineral and organic volatile and non-volatile forms.

Mobility. To fulfill data requirements, the registrant submitted a published non-FIFRA, non-GLP study by Wauchope (Wauchope, 1975) for Agency review (part of 27 June 1986 review package, EPA Accession No. 260061). Wauchope measured the simple batch equilibrium adsorption of 16 Mississippi River alluvial flood plain soils, none of which were in the "sand" textural class, two of which had a "clay" texture, and 14 of which had a "loam" texture. The main study objectives were to correlate sorption with soil properties and to make direct experimental comparison of the relative sorptions of phosphate (as $H_2PO_4^{1-}$, a relatively immobile soil chemical), cacodylate/cacodylic acid, arsenate/arsenic acid, and methylarsonate/methylarsonic acid (at an adjusted pH of 5.6 for all soils and chemicals). Phosphate, a large magnitude agricultural, industrial, and naturally occurring mineral with established relative immobility, is a well-suited benchmark for comparing the suite of arsenicals. Phosphorous and arsenic are also adjacent periodic table congeners in the classical or traditional family grouping VA. Wauchope did not explicitly calculate sorption coefficients.

From Wauchope's data, the Agency calculated simple soil sorption coefficients (Kd) for cacodylate at an initial cacodylate concentration of 3.2×10^{-4} M (44 ppm). The Kds ranged from 8.2 to 33 mL/g, with a median of 16 mL/g (see study summaries attachment for table of values), and were relatively independent of organic matter content. (Pseudo organic carbon sorption coefficients (Koc) range from around 700 to 7000 mL/g oc, but do not correlate with the Kd values given above.) Wauchope found that sorption was best correlated with clay and iron and aluminum oxide content. In this respect, the two organic arsenicals behaved like the inorganic arsenate and phosphate. By direct comparison with phosphate, the other three chemicals were more strongly sorbed than phosphate in the increasing order:

phosphate < cacodylate < arsenate $\underset{\sim}{}$ methylarsonate.

pH could have a major influence on sorption because of the anionic nature of the tested chemicals. Because Wauchope experimentally fixed the pH at 5.6 for the 16 soil/water systems (natural soil pHs ranged from 4.8 to 7.6), correlation with pH cannot be determined from this study. Since cacodylic acid is a weak acid with an equilibrium constant (Ka) of 6.8×10^{-7} (pKa = 6.2), at pH 5.6 the molar concentration of cacodylate anion is 21% of the total molar arsenic concentration with a corresponding neutral cacodylic acid concentration of 79% of the total. At a pH of 8.5 (near the upper end of the "environmentally relevant" range), the ratio of cacodylate to cacodylic acid is 215/1 which means the cacodylate anion represents 99.5% and cacodylic acid only 0.5% of the total molar concentration of arsenic. Generally, anionic (negatively charged) species tend to be less strongly sorbed by soil surfaces which tend to maintain a negative (repelling) charge; the surface charge also tends to increase (become more negative) at higher pHs. Thus, at more nearly neutral or alkaline pHs, sorption coefficients could be considerably lower than those given above, and mobility correspondingly higher. A recent publication on arsenate and arsenite sorption in Australian soils (Smith et al., 1999) provides some insight on the potential degree of importance of pH on sorption of acid and anion couples. Although somewhat tenuous, Wauchope's four species might be considered a homologous series with the congeners phosphorus or arsenic at the central core. Therefore, Smith's arsenate and arsenite data would serve as a relational link to the possible effect of pH on the mobility of cacodylic acid/cacodylate.

In four soils selected to vary widely in chemistry and mineralogy, Smith did indeed show that in the experimentally adjusted pH range of 2.0 to 8.5 (adjusted with dilute nitric acid or sodium hydroxide) and ionic strength range of 0.003 to 0.3 mol/L (adjusted with sodium nitrate) there are complicated pH and ionic strength dependencies. However, the Agency observes from the data in the more environmentally relevant range of pHs from 5 to 8.5 and ionic strength of 0.003 molar, that arsenate decreased in sorption with increasing pH by a maximum factor of only approximately two. This decrease is not dramatic compared with the much larger variability in simple, standard sorption Kds which Wauchope measured above and which Smith measured for a total of 10 soils (the four for the detailed pH and ionic strength dependencies plus six others for a rudimentary subset for Kd measurement and soil correlations). Smith's simple Kds for arsenate in the 10 soils were distributed in the range from 1.7 to 62 L/kg.

Although Smith did not report any calculated sorption coefficients for arsenite, his comments and plotted data of sorbed amounts show arsenite to be moderately less sorbed than arsenate. However, in contrast with the *decreasing* sorption of arsenate in the four soils in the pH range of 5 to 8.5 and ionic strength of 0.003 M, sorption of arsenite in two soils (apparently the study authors tested only two of the four soils tested for arsenate sorption) was fairly constant from approximately pH 2 to pH 5, but *increased* significantly from approximately pH 5 to the maximum reported pH 7 for arsenite. Sorption increased by a maximum factor of approximately five in the most sensitive of the two soils. Effect of ionic strength on sorption of arsenite was small and complex in the tested ranges of pH and ionic strength.

Overall, the Agency concludes from Smith's surrogate data in the more environmentally relevant range of pHs from 5 to 8.5 and ionic strength of 0.003 molar, that sorption of cacodylate/cacodylic acid should not decrease (increase mobility) dramatically with pH when compared to the much larger variability in soil sorption Kds in Smith's study and in Wauchope's previous study with Mississippi flood plain soils.

Ground Water. On a comparative basis with the established relative immobility of phosphate, any leaching of the tested arsenicals to ground water caused by the labeled use (non-point source) of cacodylic acid would not be expected to be significant. Consistent with this expectation, a supplemental field dissipation study also reasonably demonstrated that leaching should not be a significant route of dissipation.

However, to prevent any misunderstanding until further discussion below, the limited leachability of cacodylic acid should not be interpreted to mean that its use would not add *any* contribution to the *total* arsenic load in groundwater to which humans are, in fact, exposed. Only that labeled use of cacodylic acid should not contribute significantly to the already existing exposure to arsenic (including any natural cacodylic acid) in groundwater. More particularly, agricultural use of cacodylic acid would certainly not be expected to raise background groundwater concentrations of natural arsenite and arsenate more than a small fraction over a long period of time. Additional discussion which includes monitoring data from the USGS is in the separate Drinking Water Exposure Assessment section below.

Surface Water. The surface water assessment results and conclusions are different from the ground water. Erosion and runoff of surface deposits would carry cacodylic acid and other arsenic species to surface waters and sediments at concentrations which could cause local, temporal excursions above background. Potential risks associated with ecological aquatic exposure was presented in the Aquatic Exposure, Hazard and Risk section of the main body of this science chapter.

As discussed further in the Drinking Water Section, the labeled use of cacodylic acid presents the potential for increased surface drinking water exposure of humans to cacodylic acid and metabolites. Incremental concentrations in some cases appear to be roughly comparable to background, and would, therefore, crudely double local ambient concentrations. In drier areas where metabolism would be slower, there could be some build up of cacodylic acid in soil which would accentuate surface water concentrations whenever runoff occurred. Build up in soil is, of course, moderated by episodic runoff events to water bodies and sediments; by slow, vertical and horizontal gradients in soil; and by slow atmospheric dispersal of volatile arsines with their eventual transformation, redeposition, and redistribution (chemical and physical) throughout the environment as part of the natural arsenic cycle.

Bioconcentration. A low octanol/water partitioning ratio (Kow < 0.028) indicates little potential for bioconcentration of cacodylic acid. Although the scientific literature (e.g., FWS, 1988; NAS, 1977; ACS, 1975) shows that many plant and animal species (shrimp, for example) selectively have high bioconcentration factors for other organic forms of arsenic, these compounds are reported as practically nontoxic. In many species (including humans), cacodylic acid is a major, final waste product from the metabolism of arsenic compounds ingested from natural food, minerals, and water sources. The published literature also shows the absence of biomagnification.

DRINKING WATER EXPOSURE ASSESSMENT

Background and Basis.

As stated in the introduction, cacodylic acid is one of several arsenical pesticides which the Agency is or will soon be considering for reregistration. Ultimately, in another action, the Agency will assess the potential overall (aggregate, cumulative) drinking water exposure to these compounds and common transformation products. The EPA Office of Water (OW) is scheduled to issue a proposed and final regulation on the larger issue of "arsenic" in drinking water by the years 2000 and 2001, respectively.

This drinking water assessment is based primarily on 1) fate studies reviewed in the Environmental Fate Assessment Section of this document, 2) limited monitoring for cacodylic acid and other *speciated* forms of arsenic in a mixed assortment from pesticidal use or non-use areas, and 3) extensive monitoring for *total*[3] arsenic.

Although monitoring for individual chemical forms of arsenic is sparse, the available measured data are revealing. Surface water conclusions from these sources are compared with simulation model predictions. The primary monitoring sources are identified briefly as follows:

1) The United States Geological Survey (USGS) has recently completed an extensive survey report entitled "Arsenic in Ground Water of the United States: Occurrence and Geochemistry" (Welch, 1999), which is soon to be published in the journal *Groundwater*. Alan H. Welch, a principal investigator, has provided the Agency with an advance version of the report and, through telephone discussions, provided valuable insights. Water analyses were almost entirely for undifferentiated or *total* arsenic, as footnoted. Although the survey was dedicated to ground water, it also includes some useful information for surface water. In addition to survey information and statistical analysis, it provides a comprehensive bibliography and discusses the many of the facets of the biogeochemistry of arsenic.

2) A separate, limited investigation by USGS research scientists (Garbarino and Burkhardt, 1998), provided data on the arsenic species cacodylic acid, monomethylarsonate, arsenite, and arsenate in ground water <u>not</u> associated with arsenical pesticide application and in surface waters in areas which are associated with the application of MSMA, a compound closely related to cacodylic acid.

3) The EPA Pesticides in Groundwater Database (EPA, 1992) provided groundwater monitoring data for a localized area in Texas and another in the State of Washington.

4) The BASINS and STORET databases maintained by the US EPA provided a large body of data (many tens of thousands or more of entries) on *total* arsenic concentrations in surface waters of the U.S.

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[3] Typical or conventional laboratory analysis does not differentiate among the various inorganic species and organic species of arsenic. Analysis for total arsenic, of course, sets an upper bound for all arsenic containing species from all sources. Any contribution specifically from cacodylic acid would be masked.

5) Chemical speciation data published in 1973 on six fresh surface water bodies, one well, and three saline waters around Tampa, Florida, revealed background concentrations for cacodylic acid, monomethylarsonate, arsenite, and arsenate.

Groundwater Exposure

The USGS (Welch, 1999) retrieved water-quality data for about 50,000 samples from about 30,000 sample locations from the USGS's National Water Information System (NWIS, which includes National Water Quality Assessment (NAWQA) data), and additional data from many other sources. A subset of about 20,000 analyses from the years 1973-1997 which met certain criteria were selected (censored) for statistical testing. Only a single analysis for a particular well or spring was used to avoid bias towards frequently sampled sources. Sample sites were not uniformly distributed across the country and were not specifically targeted for areas where arsenical pesticides were applied. The survey authors conclude that while slightly less than half the groundwater samples had total arsenic concentrations < 1 ug/L, about 10% exceeded 10 ug/L. They further conclude that "natural" arsenic concentrations exceeding 10 ug/L are more widespread and common than previously recognized. Some areas of high arsenic concentrations
(defined as > 50 ug/L) were associated with point source pollution (for example, Superfund Sites where about 30% of approximately 1200 sites list arsenic as a "contaminant of concern"), but most appear to be natural areas. A USGS map of total arsenic distribution in ground waters of the U.S. is given in Appendix 11.

Based on a few regional studies of agricultural use of *inorganic* arsenical pesticides (not the "organic" cacodylic acid), the survey authors conclude that groundwater arsenic concentrations do not correlate well with use, and that groundwater is largely unaffected by their use in those areas (North Dakota, South Dakota, Wisconsin, Minnesota). Almost all instances of significant detections of the inorganics are associated with disposal or other types of point source pollution.

The survey authors report that even in areas that tend to have naturally high arsenic concentrations there exists some ground water with low to very low arsenic concentrations. Steep lateral and vertical concentration gradients exist, showing inherent local spatial variability. The USGS scientists state that a statistically based evaluation of these observations requires work on, among other things, development of lithochemical geologic/aquifer relationships. Similar reports of high spatial variability over small, localized areas come from scientists investigating numerous recent newsworthy instances of serious arsenic poisoning deriving from drinking water wells in India (West Bengal) and Bangladesh (Nickson, et al., 1998; Masud, 2000; numerous others).

The USGS reports few analyses of groundwater samples specifically for methylated arsenic compounds such as cacodylic acid. However, about 30 groundwater samples taken in northwestern Nevada where these compounds were <u>not</u> used were analyzed for background monomethylarsonate and cacodylic acid (also identified as dimethylarsinate). The data suggested to the authors that groundwater in areas where arsenical pesticides are <u>not</u> applied contains < 1ug/L of methylated arsenic (all analyses were < 0.3 ug/L).

In a separate study by USGS research scientists (Garbarino and Burkhardt, 1998), 6 groundwater samples from Idaho, 10 from Illinois, and 8 from Nevada (total of 24 sites) were analyzed for arsenite, arsenate, monomethylarsonate, and cacodylic acid. Again, none of the sites were associated with the application of arsenical pesticides. With a detection limit of approximately 0.2 ug/L, there were no measurable concentrations of the methylated compounds in ground water. In contrast, arsenite or arsenate concentrations in these groundwater samples ranged from less than the method detection limit of approximately 0.2 ug/L to a concentration as high as approximately 900 ug/L. Their data show that either arsenite or arsenate or both were detected in all samples, typically at 10-50 ug/L. Arsenite and arsenate concentrations were comparable. In a personal communication, one of the study authors expressed surprise at this latter comparability, since arsenate is generally assumed to dominate.

As part of a study of 10 natural waters (one ground water, nine surface waters) in the vicinity of Tampa, Florida (Braman and Foreback,1973), one water well at a remote camping area was sampled. Tampa tap water was also analyzed. Details of this study are given below in the Surface Water Exposure Section. The well water concentration for cacodylic acid was 0.4 ug/L (ppb); for methylarsonic acid, 0.2 ug/L; and for arsenate (as arsenic), 0.3 ug/L. Concentration of arsenite (as arsenic) was less than the detection limit of 0.02 ug/L (20 parts per trillion). Tampa tap water "contained only traces of arsenate".

Reported monitoring data in the EPA Pesticides in Groundwater Database show relatively high concentrations of *total arsenic* in a high percentage of water wells in localized areas of Texas [concentrations of 10-680 ppb in 91 of 247 wells with limits of detection (LODs) for most samples of 25 ppb; fewer with LODs of 10 ppb]; and in the State of Washington (1.6-13.3 ppb in 15 of 20 wells with LOD of 0.2 ppb). The Texas data (paragraph 1 below) were associated with use of cacodylic acid; the Washington data (paragraph 2 below) were not.

1) From the Texas report (Aurelius, 1988), the Agency independently concludes that these detections are not reasonably attributable to labeled pesticidal application (non-point source) of cacodylic acid or other currently used arsenicals. Rather, the high concentrations were most likely caused by cacodylic acid-treated cotton gin waste which was spread in the vicinity of poorly cased wells, and by somewhat higher natural concentrations of arsenic.

2) In Washington (Erickson, 1990), natural conditions including historical volcanic activity; strongly alkaline, sandy soils; hydrology favorable to the migration of soluble constituents; former heavy use of calcium or lead arsenates (sometimes hundreds of pounds/acre annually) in orchards; thermal waters; or wastes from mining operations may have contributed to the elevated concentrations.

<u>Groundwater Conclusion.</u> *In view of 1) the extensive USGS survey report on arsenic (principally total arsenic); 2) the limited, monitoring data for speciated arsenicals, including cacodylic acid; 3) the relative immobility of cacodylic acid indicated by laboratory sorption and comparison with phosphate; and 4) the insignificant leaching of cacodylic acid observed in a supplemental field study, it is reasonable for the Agency to conclude that highly variable background concentrations of arsenic species in groundwater (including arsenite and arsenate, the mineral allies/metabolites of cacodylic acid) should be largely unaffected by the labeled, agricultural (non-point source) use of cacodylic acid on cotton.*

This conclusion should not be interpreted to mean that humans are not exposed to arsenicals in their drinking water from groundwater sources. It is patently clear from all sources that humans are exposed to significant concentrations of chemical forms of arsenic (including cacodylic acid) in their drinking water from groundwater sources. However, labeled use of cacodylic acid should not contribute significantly to the already existing burden of arsenic in groundwater from all sources, natural and anthropogenic. Furthermore, the prevalence of so much natural total arsenic, including arsenite and arsenate, suggests that any concerns be directed toward other arsenic species. It is therefore desirable that whenever future groundwater samples are analyzed for total arsenic (as has usually been the case), that arsenic be speciated whenever total arsenic concentrations justify possible toxicity concerns.

Surface Water Exposure

As discussed under “mobility” in the environmental fate section above, eroding soil and runoff water would transport cacodylic acid and metabolites to surface waters. The extensive USGS report cited above on arsenic in ground water (which had a modicum of surface water information), as well as other sources (e.g., Hem, 1985), indicate that total arsenic concentration in the majority of U.S. rivers and streams is less than 1 ug/L. However, as for ground water, many notable exceptions of higher arsenic concentrations occur; the highest most likely to occur in geothermal areas and in water draining mineralized areas.

The BASINS and STORET databases maintained by the US EPA have a large body of data (many tens of thousands or more of entries) on *total* arsenic concentrations in surface waters of the U.S.. However, because of the wide ranging concentrations (see below) in space and time, and the multiplicity of possible major sources of arsenic, any attempt to associate these with cacodylic acid use would likely be a fruitless exercise, and would certainly require a major resource effort akin to that by the USGS for groundwater. Nevertheless, even casual inspection of the data from the databases shows that is not unusual for total arsenic concentrations in raw surface water in many different sites to be several parts per billion. (Reporting limits in many cases appear to be 1 ppb, but in many other cases are in excess of 10 ppb and up to approximately 50 ppb. The 10 and 50 ppb limits may be associated with the human health limits currently set for total arsenic set by the World Health Organization and the US EPA, respectively.)

Spatial variability is the rule. The data for Georgia and Texas given below are illustrative of this variability and are not meant to imply a special situation. For example, in Georgia, as presented in BASINS, upper 85th percentile concentrations of total arsenic at different sites ranged from less than 1 ppb to 338 ppb. More typical high values would fall in the range of 10 to 50 ppb. The most probable concentration appears to fall in the range of <1 to 2 or 3 ppb. The STORET database for Georgia and Texas show similar results, with Texas seeming to average several parts per billion more. Some of the highest values reported in STORET for Georgia and Texas (79,000 entries) approach 1000 ppb and can often be associated with past point source pollution by humans. Such pollution is becoming less serious through environmental conscientiousness and governmental regulation. However, as previously mentioned, natural sources (especially in places in the western U.S.) also produce such high concentrations. It is noteworthy that most major drinking water facilities which use surface water often use water treatment techniques (e.g., flocculation with compounds of aluminum or iron) which are generally effective in reducing total arsenic concentrations in the observed ranges to less than 1 ppb. As was established above, if desired, it is possible to measure and speciate lower concentrations.

As previously stated, data specifically on methylated forms of arsenic in surface waters are sparse. One precocious study (partially described in the groundwater section above) for 10 natural waters in the vicinity of Tampa, Florida, published in 1973 (Braman and Foreback) revealed background concentrations of cacodylic acid to range up to 1.8 ug/L. There were six surface fresh water bodies (two rivers, two ponds, two lakes), three saline waters (two bays, one tidal flat), and one water well at a remote camping area. Tampa tap water was also analyzed. Analysis was for the four arsenic species: cacodylic acid (dimethylarsenic acid), methylarsonic acid (methyl arsonate, MMA or MSMA), arsenite, and arsenate. Presumably, all water sites were sampled once with two or more replicates analyzed; however, the study authors did not report specifics on sampling dates and the number of samples analyzed or replicated. All concentrations reported below are as arsenic equivalents (to get cacodylic acid concentrations, for example, multiply all values given below for cacodylic acid by the relative chemical weights of approximately 138/75 or 1.8). [In addition to the water samples, human urine (15 ppb cacodylic acid, N=8; 3 ppb methylarsonic acid, N=8; 2 ppb arsenite, N=4; and 4 ppb arsenate, N=4), bird eggshells, seashells, and a limestone rock, were analyzed.]

Concentrations of cacodylic acid (reported as arsenic) in the natural waters ranged up to 1.0 ppb (1.0 x 1.8 = 1.8 ppb cacodylic acid). At one site, the Hillsborough River, concentrations were below a remarkably low detection limit of 0.02 ppb, while the median value for cacodylic acid (as arsenic) at the other nine sites was approximately 0.3 ppb (0.5 ppb cacodylic acid). The well water concentration, as given previously, was 0.2 ppb (0.4 cacodylic acid). Concentrations of arsenate, detected at all ten sites, were similar to cacodylic acid. Arsenite was detected at only six of the ten sites, but had the highest concentration (2.7 ppb) of all species. Methylarsonic acid, detected in eight of the ten sites, was generally present at lower concentrations, the highest being 0.22 ppb. However, in a broader sense, considering the few samples, surface water concentrations of all four were similar. Total arsenic concentrations ranged from approximately 0.3 to 3.6 ppb. The extent to which these concentrations represent the natural background in the Tampa area or are influenced by introduction of artificial sources is unknown. However, the study authors considered the sampled sites as "natural" waters. As previously given, Tampa tap water "contained only traces of arsenate".

In another arsenic speciation study, USGS research scientists (Garbarino and Burkhurdt, 1998) collected surface water samples at one or two week intervals from early March through the middle of September of 1997 from each of three sites associated with different basins or sub-basins in an agricultural region potentially impacted by application of MSMA (application is normally from May through July). MSMA can be used as a surrogate for cacodylic acid because it is chemically closely related to cacodylic acid; produces cacodylic acid as a metabolite; is a minor metabolite of cacodylic acid; and has a similar use and environmental fate profile (cacodylic acid is slightly more mobile). Sampling dates and times varied between sites and were not correlated. A total of 24 samples were analyzed from each site. Analyses were for MSMA (as the acid MMA), cacodylic acid (DMA), arsenite, and arsenate. Maximum concentrations of MMA at the three sites were approximately 2, 3, and 5 ug/L, and were relatively short-lived. *As a surrogate and with adjustment for application rates, similar concentrations would be expected for cacodylic acid.* Concentrations of cacodylic acid (a possible metabolite of MSMA), were at or below the detection limit of 0.2 ug/L, except for one sample which registered approximately 0.6 ug/L. Maximum arsenite concentrations were approximately 2, 3, and 3 ug/L. Maximum arsenate concentrations were approximately 2, 5.5, and 5.5 ug/L. The comparable concentrations of arsenite and arsenate is again noteworthy. The inorganic species generally increased later in the summer, possibly indicating alkylarsenic degradation (oxidation) or a secondary source of inorganic arsenic. However, until similar baseline data for surface water sources where no arsenicals are applied are compared, no conclusions can be reached about whether the fluctuations are part of the natural arsenic cycle or influenced by pesticide application.

It is informative to compare the preceding surface water results with environmental simulation model predictions for potential increases in surface water concentrations. The Agency has recently adapted the standard PRZM/EXAMS model for runoff to an Index Drinking Water Reservoir (IR), and also makes an allowance for an estimated maximum of surrounding land which may be cropped. Model input values specific to cacodylic acid are given in an attachment. Resulting acute and chronic drinking water concentrations for the IR scenario for cotton grown in Mississippi with one annual application of cacodylic acid at a rate of 0.60 lb/acre and with a multiplicative factor for percent cropped area (PCA) of 0.20 (20% cropped) are:

Acute (one-in-ten year peak concentration x PCA): 29 ug/L x 0.20 ~ 6 ug/L (ppb)

Chronic (one-in-ten year peak concentration x PCA): 7.0 ug/L x 0.20 ~ 1 ug/L (ppb)

Conclusion for Surface Drinking Water. Whether coincidence or not, and whatever the source, the modeled values for cacodylic acid for surface drinking water are similar to those measured and discussed above for both use and non-use areas, and would, therefore, generally represent an additional, localized burden above background. If there are toxicological concerns at or near the monitored and modeled concentrations, then, clearly, this observation invites broader scale, systematic environmental sampling and analysis for cacodylic acid and other speciated arsenicals in order to determine statistically the associations, ranges of exposure, and possible effects. As is obvious from the Florida and USGS work, adequate analytical methods for arsenical chemical speciation are available.

While all of the pesticidal arsenicals certainly can contribute to total arsenic in surface water in use areas, their additive effects would be generally comparable to the lower limits of most observed concentrations of total arsenic (including arsenite and arsenate) or a small superposition on larger collective contributions at the upper limits of concentrations from other sources, natural or anthropogenic. However, considering the speciated measurements by the USGS researchers, those by Braman and Foreback, and the similarity of model predictions, if there is concern for concentrations of cacodylic acid *per se*, then its pesticidal application clearly appears to represent an additional, localized exposure burden of magnitude comparable to background concentrations.

REFERENCES. Those not cited within the RED document provide additional background information. There are many other available references. In 1984, the U.S. Department of Agriculture Agricultural Research Service published a bibliography on *Arsenic and Arsenical Pesticides* which contained almost 3500 citations.

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APPENDIX 7

A. PRZM (3.12) SIMULATION MODEL CHEMICAL INPUTS
B. EXAMS(2.97.5) SIMULATION MODEL CHEMICAL INPUTS
C. PRZM/EXAMS INDEX RESERVOIR DRINKING WATER CONCENTRATION OUTPUTS

FOR CACODYLIC ACID

Scenario for Aerial Application in Yazoo, County, Mississippi
Loring Silt Loam Soil

A. PRZM MODEL CHEMICAL INPUTS

Application Rate (one application)	0.60 lb/acre		**0.67 kg/ha**
Aerobic Soil Metabolism (upper 90% confidence limit based on mean of five soils)	Half-life: 102 days	**Rate Const.:**	**6.73×10^{-3}/day**
Anerobic Soil Metabolism (upper 90% confidence limit based on mean of five soils)	Half-life: 168 days	**Rate Const.:**	**4.13×10^{-3}/day**
Sorption Coefficient (Kd)		**Kd:**	**8.2 mL/gram**
Incorporation Depth	No Incorporation		**0 cm**
Application Efficiency	95 percent		**0.95**
Spray Drift Fraction	16.2 percent		**0.162**

B. EXAMS MODEL CHEMICAL INPUTS

Molecular Weight			**138 grams/mole**
Solubility in Water	Very soluble		**~1 x 10^6 mg/L**
Melting Point			192-194 ^{0}C
Vapor Pressure (Torr)	Non-volatile		**0**
Henry's Law Constant (atm-m^3/mole)	Non-volatile		**0**
Hydrolysis	Does not hydrolyze	**Rate Const.:**	**0**
Photolysis	Does not photolyze (quantum yield 0)	**Rate Const.:**	**0**
Aerobic Aquatic Met. (twice the PRZM aerobic soil half-life given above)	Half-life: 4.94 x 10^3 hours	**Rate Const.:**	**1.40 x 10^{-4}/hr**
Anaerobic Aquatic Met. (twice the PRZM anaerobic soil half-life given above)	Half-life: 8064 hours	**Rate Const.:**	**8.60 x 10^{-5}/hr**
Sorption Coefficient (Kd)		**Kd:**	**8.2 mL/gram**

C. PRZM/EXAMS INDEX RESERVOIR DRINKING WATER CONCENTRATION OUTPUT

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            WATER COLUMN DISSOLVED CONCENTRATION (PPB)

YEAR      PEAK   96 HOUR    21 DAY    60 DAY    90 DAY    YEARLY
----      ----   -------    ------    ------    ------    ------
1948    10.570    10.280     9.272     8.405     7.472     3.322
1949    13.920    13.500    11.960    10.160     9.033     3.504
1950     5.252     5.091     4.576     3.910     3.429     1.747
1951    26.170    25.370    23.010    19.340    17.360     6.522
1952     4.508     4.371     3.848     3.418     3.426     2.111
1953     4.115     3.989     3.509     2.692     2.547     1.137
1954     5.096     4.940     4.344     3.823     3.372     1.837
1955     5.694     5.520     4.879     4.034     3.453     1.836
1956    11.080    10.740    10.100     8.796     7.765     2.772
1957    16.330    15.830    14.320    11.520    10.520     4.874
1958    18.830    18.250    16.490    12.900    10.930     4.465
1959    11.360    11.030     9.796     9.182     8.336     3.217
1960    44.910    43.530    38.850    30.710    26.210     9.552
1961     4.433     4.300     3.789     2.947     2.664     1.756
1962     7.481     7.252     6.684     5.641     5.044     1.966
1963    15.040    14.580    12.930    11.160     9.787     3.888
1964     7.200     6.980     6.221     5.481     5.309     2.663
1965     4.560     4.421     3.974     3.348     3.058     1.732
1966    33.660    32.870    30.880    24.040    20.090     7.161
1967     9.988     9.682     8.535     7.135     6.509     3.225
1968    17.520    16.980    14.930    12.980    11.340     4.072
1969     9.905     9.602     9.099     8.110     7.600     3.536
1970     4.242     4.112     3.618     3.361     3.009     1.595
1971    16.940    16.420    15.340    13.200    11.790     4.192
1972    13.220    12.810    11.260     9.905    10.030     4.596
1973    13.320    13.020    11.800     9.272     8.183     3.278
1974    10.390    10.070     8.859     7.510     6.571     2.692
1975    13.550    13.140    11.600     9.336     8.139     3.411
1976    18.070    17.510    15.390    11.770    10.090     3.724
1977     7.024     6.864     6.240     5.728     5.206     2.118
1978    31.210    30.480    26.980    21.650    18.850     7.451
1979     7.304     7.082     6.620     5.824     5.322     3.434
1980     4.115     3.989     3.510     2.681     2.298     1.388
1981    28.530    27.650    25.000    20.790    18.160     6.751
1982     4.353     4.237     4.049     3.343     3.347     1.855
1983     5.133     4.976     4.590     3.833     3.270     1.318

upper
10th    29.334    28.499    25.594    21.048    18.367     6.874
percentile

   MEAN OF ANNUAL VALUES =                          3.464
   STANDARD DEVIATION OF ANNUAL VALUES =            1.961
   UPPER 90% CONFIDENCE LIMIT ON MEAN =             3.948
```

Percent Cropped Area(PCA)for Cotton = 20%

Acute: **1-in-10-year peak concentration x PCA = 29.334 x 0.20 = 5.87 ug/L**

Chronic: **1-in-10 year average annual mean x PCA = 6.874 x 0.20 = 1.37 ug/L**

APPENDIX 8

GENEEC MODEL INPUT/OUTPUT TABLES FOR APPLICATION RATE OF 0.6 LB AI/ACRE FOR COTTON AQUATIC ECOLOGICAL ASSESSMENT

Cacodylic Acid **INPUT VALUES** with and without degradation
Where applicable, top values without degradation, bottom values with degradation

RATE (#/AC) ONE(MULT)	APPLICATIONS NO.-INTERVAL	SOIL Koc (Kd)	SOLUBILITY (PPM)	% SPRAY DRIFT	INCORP DEPTH(IN)
.600(.600)	1 1	707 (8.2)	2.6 x 10^6	5.0	0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS	PHOTOLYSIS (POND) (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
.00	2	N/A .00-	.00 . 00	*****	
103				*****	**206**

Cacodylic Acid **OUTPUT** GENERIC EECs (IN PPB) with and without degradation**.***
Top values without degradation, bottom values with degradation.

PEAK GEEC	AVERAGE 4 DAY GEEC	AVERAGE 21 DAY GEEC	AVERAGE 56 DAY GEEC
11	11	9.6	8.3
11	**10**	**9.2**	**7.5**

*****No significant difference over the time period with or without degradation.

APPENDIX 9

Arsenic Species Commonly Found in Environmental Samples and Cited in RED Chemical Formulas and Names

<u>"Organic" Species</u>

$(CH_3)_2AsO(OH)$	**cacodylic acid**, dimethylarsenic acid, hydroxydimethylarsine oxide
$(CH_3)AsO(OH)_2$	methanearsonic acid, methylarsonic acid
$(CH_3)_2AsH$	dimethylarsine
$(CH_3)_3As$	trimethylarsine

<u>"Inorganic" Species</u>

AsO_4^{3-}	arsenate
AsO_3^{3-}	arsenite

APPENDIX 10

ENVIRONMENTAL FATE STUDY SUMMARIES, STATUS, AND CITATIONS

Many of the studies below are from the published scientific literature, and were not necessarily conducted under FIFRA 1988 Guidelines or Good Laboratory Practices. The published metabolism studies are vital to the environmental assessment, and the only soil mobility data available are from the published literature. In the sections below, these studies are designated as "published study" and also identified by name of author and date of publication. Complete identification of published studies is given in a separate and final "CITATIONS" section.

Based on all available data, ***there are no further requirements at this time, <u>except</u> for analytical chemical methods in water and soil and their validation****. The water method should allow for limits of detection of 0.05 ppb, preferably lower, in order to adequately cover the range necessary to protect at the DWLOC of 0.49 ppb, based on a Q* cancer risk.*

1. Hydrolysis (§161-1), MRID 420592-01. Satisfied (EFED review, 16 Jan 92).

Cacodylic acid (^{14}C-labeled on one methyl group) at a concentration of approximately 2.6 ppm was *stable* (half-life indeterminately long in a 30-day test period) against hydrolysis in the dark at pHs 5, 7, and 9 at 25 C. A total of less than 2% of applied radiocarbon appeared as unidentified degradates at any time interval.

2. Photolysis in Water (§161-2), MRID 416626-01. Satisfied (EFED review, 31 Oct 91).

Cacodylic acid (^{14}C methyl-labeled) at a concentration of approximately 2.8 ppm *did not photodegrade* at 25 C in buffered pH 7 solutions exposed to sunlight with an average daily energy of 5.1 ± 2.3 watt-minutes/cm^2 for 30 days.

3. Photolysis on Soil (§161-3), MRID 416620-02. Satisfied (EFED review, 31 Oct 91).

Cacodylic acid (^{14}C methyl-labeled) at a concentration of approximately 2.8 ppm *did not photodegrade* on a sandy loam soil at 23-25 C exposed to sunlight with an average daily energy of 5.1 ± 2.3 watt-minutes/cm^2 for 30 days.

4. Aerobic Soil Metabolism (§162-1) Partially Satisfied (this document). However, no further studies are required at this time.

A. MRID 426160-01 (EFED review, 26 Nov 93).

Cacodylic acid (^{14}C methyl-labeled) at an initial soil concentration of approximately 12 ppm *did not degrade* in a sandy loam soil that was incubated in the dark for one year at approximately 25 C and 75% of field moisture capacity. [In contrast, supplemental data from other aerobic soil metabolism studies (27 Jun 86 review summarized in 4.B. below and other studies cited in section 4 below) indicated that biodegradation did occur with the release of alkyl arsines and carbon dioxide.]

B. Accession No. 259582 and associated Nos. 260061 and 260782. The summary below is an expansion of the 27 June 86 Agency review of a published laboratory study (Woolson and Kearney, 1973) which investigated both aerobic and anaerobic (flooded) soil metabolism. This study was not specifically cited as deficient in the 1986 Agency review, but certainly does not meet current guideline standards for several reasons discussed below. It does, however, in the larger context, provide useful information from the professional literature. Other aspects of this study may be integrated within the main text of the environmental fate assessment of this document.

^{14}C-cacodylic acid at three concentrations (1, 10 and 100 ppm) in each of three soils of varying iron and aluminum content was incubated in covered beakers (essentially on open system) at 25 C and 75% of field moisture capacity. Chemical analysis was for 1) total ^{14}C (not cacodylic acid *per se*) remaining in soil and for ^{14}C extracted from various soil fractions (water soluble, iron, aluminum, calcium) at all concentrations and 2) for total arsenic extracted from the soils dosed at 100 ppm only. Unidentified ^{14}C metabolites could have been in any extract, but, unfortunately, there was no chemical analysis for them. In a separate, experiment, ^{14}C carbon dioxide evolution was investigated in one soil (two treatments, soil adapted and unadapted to cacodylic acid) at a dosed concentration of 1%.

Based on ^{14}C remaining in soil after the single time interval from zero to 24 weeks after dosing at an initial cacodylic acid concentration of 100 ppm, Agency estimates of aerobic and anaerobic (flooded) soil metabolism half-lives (assuming first-order kinetics) in the three soils are approximately as follows in Lakeland loamy sand, Hagerstown silty clay loam, and Christiana clay loam soils, respectively:

> Aerobic: 16.7, 12.7, and 6.9 weeks (average of 12.1 ± 4.9 weeks with an upper 90% confidence limit on the distribution of 21.4 weeks and on the mean of the distribution of 17.5 weeks).
>
> Anaerobic: 12.3, 19.7, and 22.7 weeks (average of 18.2 ± 5.3 weeks with an upper 90% confidence limit on the distribution of 28.2 weeks and on the mean of 24.0 weeks).

These Agency estimated half-lives are based on an average of three replicates for each soil of the percentage of ^{14}C remaining after the single time interval from zero to 24 weeks after dosing, as presented in Table IV of the publication, assuming first-order kinetics. In like manner, single point estimates after 32 weeks of aerobic incubation yielded significantly longer half-lives in the Lakeland, Hagerstown, and Christiana soils, respectively, of 46.4, 34.9, and 15.1 weeks (average of 32.1 ± 15.8 weeks with an upper 90% confidence limit on the distribution of 61.9 weeks and on the mean of the distribution of 49.3 weeks). The study authors did not present analogous 32-week anaerobic data. Systematic time-series data for individual soils and individual replicates were not presented.

The study authors stated that rate of application had no appreciable effect on degradation or disappearance of cacodylic acid, but did not present specific data for initial dose concentrations of 1 and 10 ppm. However, combined average time-series data for extractable ^{14}C from soil for various intervals up to 32 weeks for all replicates for all soils at all concentrations under aerobic conditions clearly support their assertion, and yield an overall first-order regression half-life of 17.0 weeks (r-squared of 0.84, one standard deviation range of 14-21 weeks) with a 90% upper confidence limit on the regression half-life of 23.7 weeks. (The study authors did not present analogous anaerobic time-series data.)

The study authors inferred that the large losses of ^{14}C and arsenic from the soils in the primary study were caused by the evolution of carbon dioxide and volatile organo-arsenic compounds but, unfortunately, did not analyze for these putative components and provided no material balance, as would be required under current Guidelines. However, in the separate, carbon dioxide evolution experiment, the adapted and unadapted soil released 13% and 2%, respectively, of the ^{14}C from the cacodylic acid dose (1% initial concentration in soil) after 98 days. Analysis of the carbon dioxide trap (KOH) showed the absence of any ^{14}C containing arsenic compound, but there was no trap specifically for volatile arsenicals. The study authors also made additional inferences or speculations on the nature of possible inorganic and organic arsenic metabolites and their distributions and differences under aerobic and anaerobic conditions in the three soils, but these are not discussed here.

C. Accession No. 259582 and associated Nos. 260061 and 260782. Other aspects of this study may be integrated within the main text of the environmental fate assessment of this document.

Based on another published study (Woolson et al., 1982), residual cacodylic acid averaged approximately 15-30% of the initial concentration of approximately 18 ppm (10 ppm arsenic) after 60 days of aerobic incubation at 25 ^{0}C in a Mattapeake silt loam soil treated under several different conditions of soil moisture (77-230% of field capacity) with unamended soil and with a variety soil amendments (equivalent to 50-100 tons/ha). Results were similar under all conditions. Based on these published data the registrant correctly estimated an average aerobic soil half-life (assumed first-order) for all amended treatments to be approximately 31 days. The estimated half-life from unamended soil was approximately 20 days.

D. Accession No. 259582 and associated Nos. 260061 and 260782. Other aspects of this study may be integrated within the main text of the environmental fate assessment of this document.

Based on yet another published Woolson paper (Woolson, 1977) with the same initial cacodylic acid concentration as the 1982 study of approximately 18 ppm (10 ppm arsenic) with the same Mattapeake soil amended with about 6% ground soybean meal and with a soil moisture content of only 25-30% of field capacity, the registrant correctly calculated an extrapolated aerobic soil half-life (based on 82% of cacodylic acid remaining after 160 days of aerobic incubation) to be roughly 1.5 years (559 days). In the same study, the analogous, extrapolated anaerobic soil half-life (based on approximately 92% remaining after 160 days at the same soil moisture content, but with a nitrogen atmosphere), would be roughly 4 years. The higher organic matter and low moisture conditions would not be typical of most agriculture.

E. The published study by Gao and Burau (Gao, 1997).

This is an important, expanded study which is atypical of the standard study which the Agency usually receives. It provides a detailed basis for the systematic understanding of four major factors which influence the aerobic soil metabolism of cacodylic acid. Results help to unify seemingly disparate results of other studies, some of which the authors review briefly. Rather than present a lengthy, redundant summary here, the study is integrated and discussed at length in the main text of the environmental fate assessment.

3. **Anaerobic Soil Metabolism (§162-2),** Accession No. 259582 and associated Nos. 260061 and 260782. Other aspects of this study may be integrated within the main text of the environmental fate assessment of this document.. Partially Satisfied (this document). However, no further studies are required at this time.

A. Since the published 1973 Woolson study (4B above) had both aerobic and anaerobic (flooded) soil components, these are summarized together in 4B. Other aspects of this study may be integrated within the main text of the environmental fate assessment of this document.

B. Likewise, since the published 1977 Woolson, et al. study (4D above) had both aerobic and anaerobic (nitrogen atmosphere, low soil moisture) components, these are summarized together in 4D above. Other aspects of this study may also be integrated within the main text of the environmental fate assessment of this document.

4. Anaerobic Aquatic Metabolism (§162-3), MRID 425726-01 (EFED review, 26 Nov 93). Partially Satisfied (this document). However, no further studies are required at this time.

Cacodylic acid (^{14}C methyl-labeled) at an initial system concentration of approximately one ppm was *stable* in a flooded clay loam pond sediment that was incubated under anaerobic conditions (nitrogen atmosphere) in the dark at 25 C for one year. [In contrast, supplemental data from previous anaerobic soil metabolism studies (27 Jun 86 review summarized in 5. above) indicated that biodegradation did occur with the release of alkyl arsines.]

5. Aerobic Aquatic Metabolism (§162-4), MRID 430361-01 (EFED review, 11 Oct 94). Partially Satisfied (this document). However, no further studies are required at this time.

Cacodylic acid (^{14}C methyl-labeled) at a concentration of approximately 12 ppm *did not degrade* in a sandy loam soil that was flooded with aerated water and incubated in the dark at approximately 25 C for 30 days.

6. Mobility (§163-1). Satisfied.

A. Accession No. 260782 and associated Nos. 259582 and 260061. (EFED review, 27 Jun 86). Except for the table of sorption coefficients given below, this summary is virtually identical to that in the environmental fate assessment of the main text.

To fulfill data requirements, the registrant submitted a published study by Wauchope (Wauchope, 1975) for Agency review (part of 27 June 1986 review package, EPA Accession No. 260061). Wauchope measured the simple batch equilibrium adsorption of 16 Mississippi River alluvial flood plain soils for phosphate (as $H_2PO_4^{1-}$, a relatively immobile soil chemical), cacodylate, arsenate, and methylarsonate (at an experimentally adjusted pH of 5.6 for all soils and chemicals). None of these soils was in the "sand" textural class, two had a "clay" texture, and 14 had a "loam" texture (see table below). One of Wauchope's main objectives was to correlate the sorption with soil properties. Another was to make direct experimental comparison of the *relative* sorptions of the arsenicals with phosphate. For these purposes he did not need and did not explicitly calculate sorption coefficients, but used other indices and correlative measures.

Reviewer calculated simple soil sorption coefficients (Kd) from Wauchope's data for cacodylate at an initial cacodylate concentration of 3.2×10^{-4} M (44 ppm) ranged from 8.2 to 33 mL/g. with a median of 16 mL/g. Tabulated below for each of the soils are their texture, Kds, percent organic matter (%OM), percent organic carbon (%OC, calculated arbitrarily by dividing OM by the factor 1.74). [Previous Agency Kd calculations (1986 review), which were recorded for only 5 of the 16 soils, were incorrect.] Kds were relatively independent of organic matter content. [Pseudo organic carbon sorption coefficients (Koc) ranged from around 1000 to 7000 mL/g oc, but since they do not correlate with the Kd values given above, they are not tabluated]. Wauchope found that sorption was best correlated with clay and iron and aluminum oxide content. By direct comparison with phosphate, the other three chemicals were more strongly sorbed than phosphate in the increasing order: phosphate < cacodylate < arsenate $\underset{\sim}{}$ methylarsonate.

SOIL*	% OM	%OC	Kd
Alligator SiCL	1.98	1.14	31
Bosket VFSL	0.73	0.42	9.1
Brittain SiL	0.81	0.47	18
Dundee VFSL	1.52	0.87	16
Dundee SiL	2.02	1.16	16
Dundee SiCL	1.65	0.95	14
Dowling C	2.26	1.30	18
Forestdale SiL	0.78	0.45	33
Forestdale SiCL	2.01	1.16	17
Forestdale CL	2.93	1.68	18
Pearson SiL	1.38	0.79	13
Pearson CL	0.81	0.47	16
Tunica CL	1.55	0.89	16
Bosket SiL	1.3	0.75	12
Bosket SL	0.25	0.14	8.2
Sharkey C	4.2	2.41	33

* Si = Silt, S = Sand, C = Clay, L = Loam, VF = Very Fine

pH could have a major influence on sorption because of the anionic nature of the tested chemicals. Because Wauchope experimentally fixed the pH at 5.6 for the 16 soil/water systems (natural soil pHs ranged from 4.8 to 7.6), correlation with pH cannot be determined from this study. Since cacodylic acid is a weak acid with an equilibrium constant (Ka) of 6.8 x 10^{-7} (pKa = 6.2), at pH 5.6 the molar concentration of cacodylate anion is 21% of the total molar arsenic concentration with a corresponding neutral cacodylic acid concentration of 79% of the total. At a pH of 8.5 (near the upper end of the "environmentally relevant" range), the ratio of cacodylate to cacodylic acid is 215/1 which means the cacodylate anion represents 99.5% and cacodylic acid only 0.5% of the total molar concentration of arsenic. Generally, anionic (negatively charged) species tend to be less strongly sorbed by soil surfaces which tend to maintain a negative (repelling) charge which also tends to increase (become more negative) at higher pHs. Thus, at more nearly neutral or alkaline pHs, sorption coefficients could be considerably lower than those given above and mobility correspondingly higher. A recent publication on arsenate and arsenite sorption in Australian soils (Smith et al., 1999, see 8B below) provides a link to the possible pH dependence and a bridge to the comparative data of Wauchope for cacodylate.

B. Publication by Smith et al., 1999.

In four soils selected to vary widely in chemistry and mineralogy, Smith showed that in the experimentally adjusted pH range of 2.0 to 8.5 (adjusted with dilute nitric acid or sodium hydroxide) and ionic strength range of 0.003 to 0.3 mol/L (adjusted with sodium nitrate) that there are complicated pH and ionic strength dependencies on the simple batch equilibrium for arsenate and arsenite. Arsenate is one of arsenic anions which Wauchope (8A above) compared with cacodylate, methylarsonate, and phosphate.

In spite of sorption intricacies, which are not discussed in this document, the Agency concludes from the data in the more environmentally relevant range of pHs from 5 to 8.5 and ionic strength of 0.003 molar, arsenate decreased in sorption by a maximum factor of only approximately two. This decrease is not dramatic compared with the much larger variability in simple, standard sorption Kds which Smith measured for a total of 10 soils (the four for the detailed pH and ionic strength dependencies plus six others for a rudimentary subset of Kd measurements and soil correlations). Simple Kds for arsenate in the 10 soils were distributed in the range from 1.7 to 62 L/kg.

Although Smith did not report any calculated sorption coefficients for arsenite, his comments and plotted data of sorbed amounts show arsenite to be moderately less sorbed than arsenate. In contrast with the decreasing sorption of arsenate in the four soils in the pH range of 5 to 8.5 and ionic strength of 0.003 M, sorption of arsenite in two soils (apparently the study authors tested only two of the four soils tested for arsenate sorption) was fairly constant from approximately pH 2 to pH 5, but increased significantly from approximately pH 5 to the maximum reported pH 7. Sorption increased by a maximum factor of approximately five in the most sensitive of the two soils. Effect of ionic strength on sorption of arsenite was small and complex in the tested ranges of pH and ionic strength.

9. **Terrestrial Field Dissipation (§164-1).** Partially Satisfied. However, no further studies are required at this time.

A. MRID 413021-01 (EFED review, 31 Oct 91). Supplemental. The original document consists of several reports (field phase, lab phase, storage stability). There is also a summary submission (MRID 920150-07).

This was an eight month study on three treated subplots and one control plot of established turf growing on a Hanford sandy loam soil in the vicinity of Madera, CA. The Madera area is in a relatively dry growing region which requires irrigation for production of agricultural crops. A cacodylic acid formulation (28.4% sodium cacodylate and 4.9% cacodylic acid) was applied twice (June 23 and 28, 1988) at the intended rate of 21.5 lb of active ingredient (cacodylic acid) per acre per treatment (the actual application rate is uncertain).

The 1991 review of this study cited many deficiencies. Information which the registrant subsequently supplied, and upon which the Agency commented (26 Nov 93 review), did not overcome the shortcomings. Among these were extreme variability in all the data; sampling and sample handling irregularities; disappearance of cacodylic acid without definition of the degradation/dissipation route(s); and inadequate storage stability data for cacodylic acid and its reputed degrades.

Another observation, not clearly and directly cited in the 1991 review, was the apparent disappearance from the field of roughly 60% of immutable arsenic applied as cacodylate as revealed in Figure 2 of the original submission. Loss was from approximately 12 ppm to 5 ppm (expressed as arsenic equivalents) in the top six inches of soil, with insignificant variation in background arsenic at depths from 6 to 48 inches. [Note: Compared to the more comprehensive Figure 2, Table 10 (0-6 inch data) of the submission has errors in some of the rows for total arsenic and for arsenic from arsenate (derived by the study author by difference from total arsenic).] Although volatile alkyl arsines were putative transformation products which could have evaporated from the plots, there were no tests to verify this possibility.

In spite of deficiencies, and taken in the context of results from other published lab studies, it is possible to infer that under the experimental conditions:

1) Cacodylic acid was relatively short-lived (below detection limit of 0.5 ppm within three months post-treatment, "half-life" of roughly one to five weeks). However, twice daily irrigations from day 6 to day 36 after the second (final) application, daily irrigations between 36 days and 6 months at approximately 0.1 inch/irrigation would have provided enhanced surficial moisture conditions for accelerated chemical and biochemical activity.

2) Although leaching was not significant for any arsenic species, whether or not cacodylic acid or its allies are prone to leaching cannot be determined from this study. The little rainfall and light irrigation during the study provide ostensible evaporative conditions under which neither leaching nor runoff would be expected (that is, daily evaporation from soil and the residual turf mat would be expected to approximately balance applied irrigation). The study author provided no water balance which could have clearly demonstrated the potential for leaching (and runoff) under the treatment conditions.

3) Methyl arsonate (equivalent to the herbicide MSMA) was a minor product in the field. It was detected at 0-6 inches only at four consecutive time intervals up to 14 days following the second application. With time increasing from day -4, day 1, day 7, day 14 (1st application on day -5, 2nd application on day 0) concentrations were 0.43, 0.58, 0.40, and 0.15 ppm (expressed as arsenic equivalents). The data are unsuitable for a half-life determination, but the compound appeared to be short-lived. There was no analysis for other organic arsenicals.

4) Inorganic arsenic was not speciated. Arsenate (AsO_4^{3-}) was assumed to be the only inorganic metabolite, and was estimated indirectly by difference between measured total arsenic and the sum of the measured arsenic equivalent of organic cacodylate and methyl arsonate.

5) Considering the *prima facie* results of this study and the non-volatile nature of cacodylic acid and methyl arsonate, the most likely, but untested, possibility for loss of total arsenic would be the escape of volatile transformation products.

B. MRID 428431-01 and duplicate MRID 434853-01 for a re-submission of the same study (Cody and White, 1993.) (EFED review, 26 Nov 93). Supplemental.

This was a one year study on three treated bare ground subplots and one control plot of sandy loam soil (soil series name(s) not given) at a test site in Monterrey County, California, near Watsonville. Cacodylic acid (Cacodylate 3.25™, SC; 4.9% cacodylic acid plus 28.4% sodium cacodylate), was broadcast applied on August 26 and 31, 1991, at an intended nominal rate of 24 lb of a.i. (as cacodylic acid) per acre per application (total 48 lb/a.i./acre). The targeted 48 lb rate was reported to correspond to the (then) maximum annual labeled application rate for a turf use pattern plus approximately 10% (the actual rate during the study was not verified).

Similar to the field study discussed above, the 1993 Agency review of this study also cited major deficiencies. Foremost among these was the disappearance of cacodylic acid without determination of the degradation/dissipation route(s). Storage stability data for MSMA, a reputed soil degrade, was also an issue.

Another observation, not cited by the study authors or in the 1993 Agency review, is the apparent disappearance from the field of roughly 20-40% of immutable arsenic as revealed by analysis of Table IX of the original submission. Loss was from approximately 17 ppm to 12 ppm of applied arsenic equivalents (after background correction) in the combined soil profile for the 0-6 inch and 6-12 inch increments, with insignificant variation in background arsenic at greater sampled depths.

In spite of deficiencies, and taken in the context of results from other published lab studies, it is possible to infer that under the experimental conditions:

1) Cacodylic acid was apparently relatively short-lived. It disappeared with a calculated first-order half-life in the top 6 inches of soil of 22 days ($r^2 = 0.86$; 0-243 days data) following the second application. The data, however, exhibited highly irregular, punctuated variations.

2) Leaching was not significant for any arsenic species, with essentially no concentration increases above background at sampled depths greater than 12 inches (concentration reporting limit of 0.05 ppm for cacodylic acid and MSMA, background arsenic concentration approximately 2 ppm for all depths). The rainfall and irrigation distribution during the study on bare ground was seemingly adequate to promote leaching beyond 12 inches if there were such a tendency. Furthermore, the study was purposely sited in a soil thought to be less retentive of arsenic because of the soil's unusually low iron and aluminum mineral content. However, because the study author provided no measure of water balance for the plots (all of which had significantly different water holding capacities), the conclusion from this study of insignificant leaching potential, is likely, but not definite.

3) Methyl arsonate (equivalent to the herbicide MSMA) was a minor product (maximum soil concentration of roughly 1 ppm) at all times, and represented a maximum equivalent of roughly 3% of

applied cacodylic acid. Furthermore, even this small amount may have been an artifact of experimental procedures. The data are unsuitable for a half-life determination, but the compound appeared to be short-lived and fell below the reported detection limit of 0.05 ppm between days 125 and 182 after the final application. There was no analysis for other organic arsenicals.

4) Inorganic arsenic was not speciated, but total arsenic was measured.

5) Considering the *prima facie* results of this study and the non-volatile nature of cacodylic acid and methyl arsonate, the most likely, but untested, possibility for the major loss of total arsenic during this study would be the escape of volatile transformation products. This issue was not addressed by the study authors.

STUDY CITATIONS

1. Hydrolysis. Lawrence, B. and Kesterson, A. 1991. MRID 420592-01.

2. Photodegradation in water. Lawrence, B. and Kesterson, A. 1990. MRID 416626-01.

3. Photodegradation on soil. Jackson, S.B. and Kesterson, A. 1990. MRID 416626-02.

4. Aerobic soil metabolism

    A. Atkins, R.H. and Kesterson, A. 1992. MRID 426160-01.

    B. Woolson, Edwin A. and Kearney, Philip C., Environmental Science & Technology, Vol. 7, 47 (1973). EPA Accession Nos. 259582.

    C. Woolson, E. A., Aharonson, N., and Iadevaia, R., "Application of High-Performance Liquid Chromatography - Flameless Atomic Absorption Method to the Study of Alkyl Arsenical Herbicide Metabolism in Soil", J. Agro. & Food Chem., 30 (1982) 580. EPA Accession Nos. 259582, 260061, 260782.

    D. Woolson, E. A., "Generation of Alkylarsines from Soil", Weed Science, Vol. 25 (1977) 412.

    E. Gao, Suduan and Burau, Richard G., "Environmental Factors Affecting Rates of Arsine Evolution from and Mineralization of Arsenicals in Soil", J. Environ. Qual., 26 (1997) 753.

5. Anaerobic soil metabolism (same as 4.B.). Woolson, Edwin A. and Kearney, Philip C., Environmental Science & Technology, Vol. 7, 47 (1973). EPA Accession No. 259582.

6. Anaerobic aquatic metabolism. Mobley, S.G., Kesterson, A., Atkins, R.H., and Lawrence, L. 1992. MRID 425726-01.

7. Aerobic Aquatic Metabolism. Atkins, R.H. 1993. MRID 430361-01.

8. Mobility (batch equilibrium).

    A. Wauchope, R.D., "Fixation of Arsenical Herbicides, Phosphate, and Arsenate in Alluvial Soils", J. Environ. Qual., Vol. 4, no. 3 (1975) 355-358. Accession No. 260782 and associated Nos. 259582 and 260061.

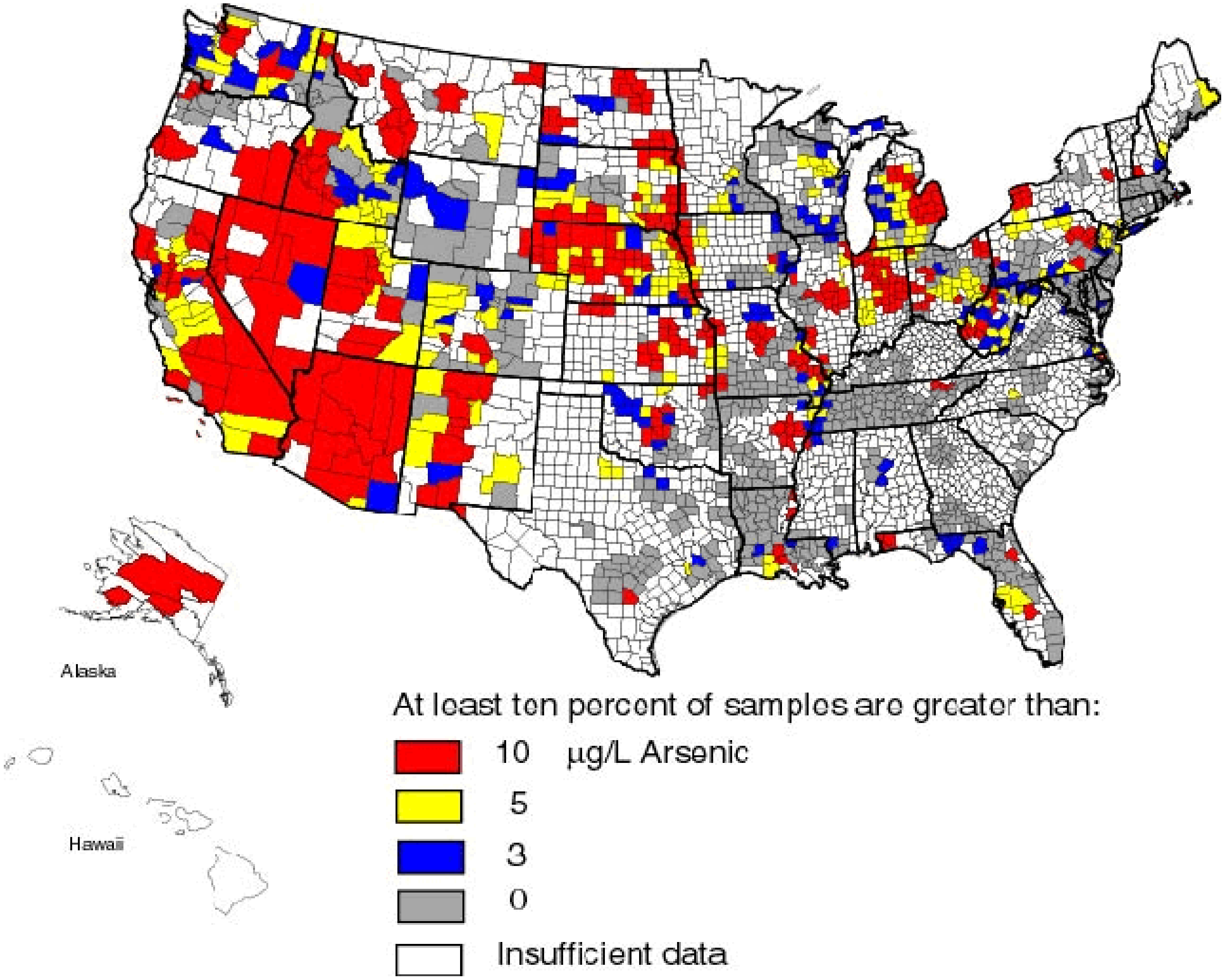
B. Smith, E., Naidu, R., Alston, A.M.. 1999. Chemistry of Arsenic in Soils: I. Sorption of Arsenate and Arsenite by Four Australian Soils. J. Environ. Qual., 28: 1719-1726.

9. Field dissipation

A. 413021-01. Woolson, 1989, on actual turf.

B. 428431-01. Coody and White, 1993. Bare ground "simulating" turf.
434853-01. Same as 428431-01 immediately above, but resubmitted with a new MRID assigned.

APPENDIX 11



ARSENIC IN GROUND WATER

USGS DATA

http://co.water.usgs.gov/trace/pubs/usgs_as_county.jpeg

Printed 2 March 2000

APPENDIX 12

Chemical No: 012501

STATUS OF DATA REQUIREMENTS FOR CACODYLIC ACID

Data Requirement	Use Pattern[1]	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
§158.490 WILDLIFE AND AQUATIC ORGANISMS				
71-1(a) Acute Avian Oral, Quail/Duck		yes	41608304	no
71-2(a) Acute Avian Diet, Quail		yes	42551301	no
71-2(b) Acute Avian Diet, Duck		yes	42551302	no
71-3 Wild Mammal Toxicity				
71-4(a) Avian Reproduction Quail		no		yes
71-4(b) Avian Reproduction Duck		no		yes
71-5(a) Simulated Terrestrial Field Study				
71-5(b) Actual Terrestrial Field Study				
72-1(a) Acute Fish Toxicity Bluegill		yes	41748302; 40098001	no
72-1(b) Acute Fish Toxicity (TEP)				
72-1(c) Acute Fish Toxicity Rainbow Trout		yes	41748301	no
72-1(d) Acute Fish Toxicity Rainbow Trout (TEP)				
72-2(a) Acute Aquatic Invertebrate		yes	41747901; 40098001	no
72-2(b) Acute Aquatic Invertebrate (TEP)				
72-3(a) Acute Est/Mar Toxicity Fish		yes	42433301; 40228401	no
72-3(b) Acute Est/Mar Toxicity Mollusk		yes	42468101; 40228401	no
72-3(c) Acute Est/Mar Toxicity Shrimp		yes	42433302	no
72-3(d) Acute Est/Mar Toxicity Fish (TEP)				
72-3(e) Acute Est/Mar Toxicity Mollusk (TEP)				
72-3(f) Acute Est/Mar Toxicity Shrimp (TEP)				
72-4(a) Early Life Stage Fish				
72-4(b) Life Cycle Aquatic Invertebrate		no		yes
72-5 Life Cycle Fish				
72-6 Aquatic Organism Accumulation				
72-7(1) Simulated Aquatic Field Study				
72-7(b) Actual Aquatic Field Study				

Data Requirement	Use Pattern[1]	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
§158.540 PLANT PROTECTION				
122-1(a) Seed Germ.,Seedling Enmergence				
122-2 Aquatic Plant Growth				
122-1(a) Seed Germ./Seedling Emerg.				
122-1(b) Vegetative Vigor				
123-1(a) Seed Germ./Seedling Emerg.		yes	41732301	no
123-1(b) Vegetative Vigor		yes	41732302	no
123-2 Aquatic Plant Growth		yes	41791101-05	no
124-1 Terrestrial Field Study				
124-2 Aquatic Field Study				
§158.490 NONTARGET INSECT TESTING				
141-1 Honey Bee Acute Contact		yes	41608310	no
141-2 Honey Bee Residue on Foliage				
141-5 Fueld Test for Pollinators				
§158.290 ENVIRONMENTAL FATE				
<u>Degradation Studies-Lab:</u>				
161-1 Hydrolysis		yes	42059201	no
161-2 Photodegradation In Water		yes	41662601	no
161-3 Photodegradation On Soil		yes	41662002	no
<u>Metabolism Studies-Lab:</u>				
162-1 Aerobic Soil		partially	42616001, Acc#s 259582, 260061, 260782, published studies	no
162-2 Anaerobic Soil		partially	Acc#s 259582, 260061, 260782	no
162-3 Anaerobic Aquatic		partially	42572601, Acc#s 259582, 260061,260782,pub. studs.	no
162-4 Aerobic Aquatic		partially	43036101	no
<u>Mobility Studies:</u>				
163-1 Leaching-Adsorption/Desorption		yes	Acc#s 260782, 259582, 260061, published studies	no
<u>Dissipation Studies-Field:</u>				

Data Requirement	Use Pattern[1]	Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
164-1 Soil		partially	41302101 and summary 92015007; Duplicates: 42843101 and 43485301	no
<u>Accumulation Studies:</u>				
165-4 In Fish				
<u>Ground Water Monitoring Studies:</u>				
166-1 Small-Scale Prospective				
§158.440 SPRAY DRIFT				
201-1 Droplet Size Spectrum				
202-1 Drift Field Evaluation				

FOOTNOTES: 1. 1=Terrestrial Food; 2=Terrestrial Feed; 3=Terrestrial Non-Food; 4=Aquatic Food; 5=Aquatic Non-Food(Outdoor);6=Aquatic Non-Food (Industrial);7=Aquatic Non-Food (Residential);8=Greenhouse Food; 9=Greenhouse Non-Food;10= Forestry; 11=Residential Outdoor; 12=Indoor Food; 13=Indoor Non-Food; 14=Indoor Medicinal;15=Indoor Residential.