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Monosodium Methanearsonate (MSMA) Preliminary Work Plan

Registration Review: Initial Docket Case Number 2395

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Approved by: Personal Matters / Ex. 6

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MSMA Preliminary Work Plan – Table of Contents

Overview	**3**
Anticipated Data Needs	**4**
Statutory and Regulatory Authority	**5**
Chemical Facts	**6**
Use and Usage Information	**6**
Recent Actions	**7**
Anticipated Risk Assessments for Registration Review	**9**
Timeline	**11**
Next Steps	**11**
Appendix – Additional Areas Considered in MSMA's Registration Review	**12**

References:

This Preliminary Work Plan summarizes the Environmental Protection Agency's current position based on the following documents:

1. *Registration Review: Preliminary Problem Formulation for Monosodium Acid Methanearsonate (MSMA).* James Hetrick, Melissa Panger. March 12, 2013.

2. *Monosodium Methanearsonate (MSMA): Revised Registration Review Scoping Document for Human Health Assessments.* Donald Wilbur, Nancy McCarroll, Shalu Shelat. March 19, 2013.

3. *BEAD Chemical Profile for Registration Review: Methanearsonic acid, salts (MSMA) (013803).* Bill Phillips, Sepehr Haddad, John Faulkner. May 31, 2013

4. *Methanearsonic Acid, Salts (MSMA, DSMA, and CAMA): Review of Human Incidents.* Shana Recore, Elizabeth Evans. November 7, 2012.

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These and other supporting documents for the MSMA registration review case may be found in the docket EPA-HQ-OPP-2013-0107 at http://www.regulations.gov.

OVERVIEW

The docket for MSMA is now open, initiating the first public comment period for this registration review (docket number EPA-HQ-OPP-2013-0107). MSMA is broad spectrum, organic arsenical herbicide registered for use to control grasses and broadleaf weeds in cotton and turf (i.e. golf courses, sod farms, and highway rights-of-way). MSMA cannot be used in Florida, except for on cotton in certain counties. The remaining uses on turf were to be phased out and prohibited after December 31, 2013 according to a 2009 Agreement in Principle with the technical registrants. However, the 2009 Agreement also provided for a scientific peer review related to the carcinogenic mode of action (MOA) of inorganic arsenic (iAs), prior to the final phase-out of the remaining MSMA turf uses. In light of a Congressional directive to the National Academy of Sciences (NAS) (House Report 112-151 accompanying HR 2584) to evaluate the carcinogenic mode of action of inorganic arsenic, EPA and the MSMA registrants recently agreed to modify the 2009 Agreement (letter from Richard P. Keigwin Jr., Director, Pesticide Re-evaluation Division, to Lynn Bergeson on behalf of the Organic Arsenical Products Task Force, dated Sept. 14, 2012) to include the NAS as a potential peer review body. It is EPA's current intention to rely on the NAS for the peer review of the mode of action, although EPA retains the right to utilize either of the Agency's scientific peer review bodies (Science Advisory Board or FIFRA Science Advisory Panel) if it later determines that utilization of an Agency peer review body would be more appropriate. The NAS final report is currently scheduled to be completed in late 2015. Therefore, EPA will postpone any decision regarding the phase-out of the uses of MSMA on golf courses, sod farms, and highway rights-of-way until the NAS review is complete and the Agency has analyzed and responded to the NAS report. The Agency documents discussed above can be found in the Organic Arsenicals; Amendment to Reregistration Eligibility Decision docket EPA-HQ-OPP-2009-0191. This Preliminary Work Plan (PWP) document explains what EPA's Office of Pesticide Programs knows about MSMA, highlighting anticipated data and assessment needs, identifying the types of information that would be especially useful to the Agency in conducting the review, and providing an anticipated timeline for completing MSMA's review.

The registration review process was designed to include a public participation component to solicit input from interested stakeholders. The Agency intends, by sharing this information in the docket, to inform the public of what it knows about MSMA and what types of new data or other information would be helpful for the Agency to receive as it moves toward a decision on MSMA. The Agency encourages all interested stakeholders to review the PWP and Appendix and to provide comments and additional information that will help the Agency's decision-making process for this chemical. In addition to general areas on which persons may wish to comment, there are some areas identified in the PWP and Appendix about which the Agency specifically seeks comments and information. Interested stakeholders could include: environmental non-profit or interest groups; pesticide manufacturers; agricultural labor or commodity groups; commercial, institutional, residential, and other users of pesticides; or the public at large.

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The Preliminary Work Plan begins by listing the anticipated data needs for MSMA. Next, it discusses the statutory and regulatory authority for Registration Review. Then the document provides MSMA's chemical facts, use and usage information, recent actions, the anticipated risk assessments, and a projected registration review timeline. Finally, the Appendix to this document includes identification and discussion of some areas that are considered generally in registration review along with some additional chemical case-specific information.

ANTICIPATED DATA NEEDS

Table 1 below summarizes anticipated data needs for MSMA. For additional discussion of the anticipated data needs, see the documents *Registration Review: Preliminary Problem Formulation for Monosodium Acid Methanearsonate (MSMA)* and *Monosodium Methanearsonate (MSMA): Registration Review Scoping Document for Human Health Assessments.*

Table 1: Anticipated Data Needs for MSMA's Registration Review

Guideline Number	Study Title	Test Material	Estimated Timeframe (Months from receipt of DCI)
835.4300	Aerobic aquatic metabolism[1]	TGAI or PAIRA; Methylated arsenics (V)	24
850.1300	Aquatic invertebrate life cycle (freshwater)	TGAI; Methylated arsenics (V)	12
850.1350	Aquatic invertebrate life cycle (saltwater)	TGAI; Methylated arsenics (V)	12
850.1500	Fish life cycle (Freshwater)	TGAI; Methylated arsenics (V)	24
850.1735	Whole sediment: acute freshwater invertebrates	TGAI; Methylated and inorganic arsenics (III)	24
Non-guideline	Whole sediment: chronic freshwater invertebrates (*Hyalella* and *Chironomus*)	TGAI; Methylated and inorganic arsenics (III)	24
850.2100	Avian oral toxicity (passerine)	TGAI; Methylated arsenics (V)	12

[1] A study is under Agency review for the aerobic aquatic metabolism data requirement. This data requirement has not been included in a DCI previously, therefore it will be included in the Registration Review DCI.

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Table 1: Anticipated Data Needs for MSMA's Registration Review			
Guideline Number	**Study Title**	**Test Material**	**Estimated Timeframe (Months from receipt of DCI)**
850.2300	Avian reproduction	TGAI; Methylated arsenics (V)	24
860.1500	Crop Field trials (cotton gin byproducts) [2]	TEP	24
870.7800	Immunotoxicity	TGAI; Methylated arsenics (V)	12

TGAI = technical grade active ingredient; PAIRA = Pure Active Ingredient Radio Labeled; TEP = typical end-use product.

STATUTORY AND REGULATORY AUTHORITY

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides distributed or sold in the United States (U.S.) generally must be registered by the Environmental Protection Agency (EPA or the Agency), based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided on EPA's website[3].

The Agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The regulations governing registration review begin at 40 CFR 155.40. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial comment period, the Agency will develop a Final Work Plan (FWP) and anticipated schedule for the registration review of MSMA.

Table 2 provides a summary of the current regulatory status of MSMA.

[2] The data requirement for crop field trials for cotton gin byproducts has not been included in a DCI previously; therefore it will be included in the Registration Review DCI.
[3] http://www.epa.gov/oppsrrd1/registration_review/

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Table 2: MSMA CHEMICAL FACTS	
PC code	013803
Case Number	2395
CAS Number	2163-80-6
Year first registered	1960's
Pesticide Type	Herbicide
Chemical class	Organic Arsenical
Reregistration Eligibility Decision (RED)	August 10, 2006, amended April 28, 2009
Tolerance Reassessment Eligibility Decision (TRED)	Not Applicable
Cumulative group	Not Applicable – EPA has not made a finding that there is a common mechanism of toxicity between MSMA and other substances.
40 CFR Citation	Tolerances for MSMA are established in 40 CFR §180.289.
Dual-use	Conventional pesticidal uses only.
Non-pesticidal uses	No non-pesticidal uses of MSMA.
Pesticide Re-evaluation Division, Chemical Review Manager	Garland Waleko, waleko.garland@epa.gov, (703) 308-8049
Registration Division, Product Manager	Kable Davis, davis.kable@epa.gov, (703) 306-0415

USE AND USAGE INFORMATION

Table 3 summarizes the use and usage information for MSMA. Please see the *BEAD Chemical Profile for Registration Review: Methanearsonic acid, salts (MSMA) (013803)* in the registration review docket for more details.

Table 3: USE AND USAGE INFORMATION	
Summary of Use	MSMA is a broad-spectrum, post-emergent, organic arsenical herbicide registered for use to selectively control grasses and broadleaf weeds in cotton and turf grass. Palmer amaranth is a target weed in cotton crops. The mode of action is unknown but is suspected to be disruption followed by destruction of plant cell membranes.
Use Sites	MSMA is currently registered for use on cotton and turf (*i.e.*, golf courses, sod farms, and highway rights-of-way). The turf grass uses have significant restrictions specified, such as buffers, number of applications, and spot treatments. MSMA cannot be used in the state of Florida, except for on cotton in the following counties: Calhoun, Columbia, Escambia, Gadsden, Hamilton, Holmes, Jackson, Jefferson, Okaloosa, Santa Rosa, Suwannee, Walton, and Washington.

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Summary of Usage	Private market usage data from 2000-2010 indicates that usage averaged approximately one million pounds of active ingredient for 850,000 acres treated. For 2006-2010, cotton (89%) and pastureland (10%) accounted for the major uses (lbs/a.i. applied), with 1% applied to citrus, nuts, wine grapes, and apples. For 2007-2010, the total area treated (TAT) increased, but the lbs/a.i. leveled off for non-cotton uses (after 2009) while it increased for cotton. Use since the 2009 agreement in principle cannot yet be quantitatively evaluated, but an initial look at 2009-2010 data indicates that there does not appear to be a dramatic change in use (TAT or lbs/a.i.).
Formulation Type(s)	Emulsifiable concentrate, flowable concentrate, granular, and ready to use.
Application Method(s)	Products can be applied as a foliar treatment, soil treatment, and by aerial application.
Technical Registrant(s)	Luxembourg-Pamol and Drexel
No. of Registrations	10 Section 3 products[4]
Restricted Use	No

Guidance for Commenters: Additional areas of *use and usage related information* requested for this registration review, and of particular interest to EPA, are described below.

- Certain MSMA labels are unclear with respect to application parameters like maximum application rates, frequency of application, application intervals, and maximum number of applications per season. The Agency will work with registrants and the Organic Arsenicals Product Task Force to clarify MSMA product labels. EPA expects to approximate those parameters that remain unknown in order to conduct a quantitative assessment for MSMA.
- Confirmation of the above label information, in addition to: sites of application, formulations, application methods and equipment, and geographic limitations on use.
- Use distribution (*e.g.*, acreage and geographical distribution of relevant use sites).
- Median and 90th percentile reported use rates (lbs ai/A) from usage data – national, state, and county.
- Application timing (date of first application and application intervals) – national, state, and county.
- Foreign technical registrants not listed above who supply technical MSMA to the US market.

RECENT ACTIONS

In 2006 a Reregistration Eligibility Decision (RED) was completed for the organic arsenicals monosodium methanearsonate (MSMA), disodium methanearsonate (DSMA), calcium acid methanearsonate (CAMA), and cacodylic acid and its sodium salt. In the RED document it was determined that all uses of the organic arsenicals (i.e., CAMA, cacodylic acid, DSMA, and MSMA) were ineligible for reregistration.

[4] Section 3 product labels can be obtained from the Pesticide Product Label System (PPLS) website (http://oaspub.epa.gov/pestlabl/ppls.home).

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In 2007 and 2008, EPA received additional information that was previously not available on organic arsenicals. Data were submitted that indicated that no residues of inorganic arsenic are likely to remain in the meat and milk of animals fed cottonseeds that have been grown in fields treated with MSMA, or in food crops that are rotated with cotton that has been treated with MSMA. Cotton growers also documented the increasing spread of a weed called Palmer amaranth that is reported to be resistant to glyphosate and for which there are currently no alternative herbicides that provide adequate control of this pest. This weed reportedly can reduce cotton yields by nearly 25 percent and could significantly impact conservation tillage efforts.

In January 2009, EPA reached an agreement in principle with the technical registrants of MSMA to eliminate, phase out, and/or modify certain MSMA uses. EPA agreed to reregister the MSMA form of organic arsenicals only for use on cotton. In addition, the use of MSMA in commercial sod production, golf courses and highway right-of-ways was scheduled to be phased out by December 2013.

In September 2009, EPA issued a cancellation order that terminated all MSMA use on athletic fields, parks, residential lawns, forestry, non-bearing fruit and nut trees, and citrus orchards. The order also cancelled all remaining products containing DSMA, CAMA, cacodylic acid and its sodium salt (FRL-8422-6).

A part of the January 2009 agreement in principle provided that, before the cancellations of golf course, sod farms and highway rights-of-way uses of MSMA would take effect, EPA would convene a public scientific peer review process that would address the mode of action for carcinogenic effects of inorganic arsenic. EPA would then make a written determination as to whether EPA believes that the science on the mode of action has changed sufficiently to warrant the continued registration of those uses.

In light of a Congressional directive (House Report 112-151 accompanying HR 2584) to the National Academy of Sciences (NAS) to evaluate the carcinogenic mode of action of inorganic arsenic, EPA and the arsenic registrants recently agreed (letter from Richard P. Keigwin Jr., Director, Pesticide Re-evaluation Division, to Lynn Bergeson on behalf of the Organic Arsenical Products Task Force dated Sept. 14, 2012) to modify the Agreement to include the NAS as a potential peer review body. It is EPA's current intention to rely on the NAS for the peer review of the mode of action, although EPA retains the right to utilize either of the Agency's scientific peer review bodies (Science Advisory Board or FIFRA Science Advisory Panel) if it later determines that utilization of an Agency peer review body would be more appropriate. The NAS final report is currently scheduled to be completed in late 2015.

Therefore, EPA will postpone any decision regarding the phase-out of the use of MSMA on golf courses, sod farms, and highway rights-of-way until the NAS review is complete and the Agency has analyzed and responded to the NAS report. The Agency documents discussed above can be found in the Organic Arsenicals; Amendment to Reregistration Eligibility Decision docket EPA-HQ-OPP-2009-0191.

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ANTICIPATED RISK ASSESSMENTS FOR REGISTRATION REVIEW

The most recent comprehensive human health risk assessment for MSMA was completed in preparation for the Reregistration Eligibility Decision. The most recent ecological and environmental fate risk assessment was also completed in 2006 as an addendum to the ecological risk assessment conducted for the RED published the same year. Findings and conclusions from these risk assessments are summarized in the *Registration Review: Preliminary Problem Formulation for Monosodium Acid Methanearsonate (MSMA)* and *Monosodium Methanearsonate (MSMA): Registration Review Scoping Document for Human Health Assessments.*

During registration review, the Agency anticipates the need to conduct a comprehensive ecological risk assessment, including an endangered species assessment, for all uses of MSMA. For human health, EPA anticipates the need to conduct revised dietary, residential, and occupational risk assessments during registration review. If toxicological endpoints or points of departure are revised based on the data that are anticipated to be required for registration review, they will be considered in the new assessments, as well as any changes to the standard operating procedures or default exposure assumptions.

Table 4 below summarizes the anticipated registration review risk assessments based on the EFED Problem Formulation and HED Scoping Document.

Table 4: Anticipated Risk Assessments for MSMA's Registration Review		
Type of Risk Assessment	**Conduct?**	**Notes**
Ecological and Environmental Fate		
Comprehensive ecological (species to be assessed include terrestrial and aquatic organisms), including endangered species	Y	Arsenic speciation was not quantitatively considered in the Reregistration Eligibility Assessment (RED) for MSMA and DSMA, but will be considered in this updated assessment.
Incidents	N	A formal review is not planned, but the agency will continue to monitor incident data throughout registration review. For a discussion of MSMA's reported ecological incidents, see page 17 of the Problem Formulation.
Human Health		
Dietary		
Food	Y	These assessments may be required, and would use existing data for monomethylarsonic acid, dimethylarsinic acid, and iAs; the most updated information and policies, revised points of departure (PoDs) or uncertainty factors including any NAS Review revised cancer MoA; updated consumption information and the latest dietary exposure model; and updated estimated drinking water concentrations (EDWC's).
Drinking water	Y	

ED_002435_00006468-00009

Occupational		
Handlers (mixers, loaders, applicators)	Y	An updated assessment may be required due to changes to the use pattern and revisions to scenario specific surrogate handler exposure data since the assessment done for the RED.
Post-application	Y	An updated dermal assessment may be necessary. A quantitative post-application inhalation exposure assessment is not required at this time; however, if new policies and procedures are put into place to incorporate volatilization of pesticides as a potential source of post-application inhalation exposure, the need for this assessment may be revisited.
Residential		
Handlers Post-application	Y	A revised non-cancer assessment may be required that includes post-application exposure to treated golf courses and will incorporate as necessary updated SOP's, human factor assumptions, and currently registered use patterns. The need for spray drift and volatilization assessments will also be evaluated.
Other		
Aggregate	Y	Evaluates the combined risk from dietary and residential exposures. This assessment may be required because of the potential for short-term residential post-application exposure from the golf course use. Updated PoDs, uncertainty and safety factors, and drinking water assessment revisions and residential assessment findings will be incorporated.
Cumulative	N	At this time, EPA does not have available data to determine whether MSMA has a common mechanism of toxicity with other substances.
Tolerances	N	The current tolerance expression as listed in the 40 CFR § 180.289(a) will need to be revised to reflect product cancellations following the 2006 RED and subsequent agreements with the registrants. These changes are detailed in the *Monosodium Methanearsonate (MSMA): Registration Review Scoping Document for Human Health Assessments.*
Incidents	N	A formal review is not planned, but the agency will continue to monitor incident data throughout registration review. For a discussion of MSMA's reported human incidents, see page 11 of the Scoping Document.

Guidance for Commenters: Additional *ecological information* requested for this registration review, and of particular interest to EPA, is described below.

- Thermodynamic data pertaining to the methylation/demethylation of arsenic, as well as information on speciation modeling of the methylation/demethylation of arsenic in aquatic and soil environments.
- Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency.
- Water quality monitoring data (see Appendix for further details).

TIMELINE

EPA has created the following estimated timeline for the completion of MSMA's registration review in Table 5 below.

Table 5: Projected Registration Review Timeline	
Activities	Estimated Date
Opening the Docket	
Open Docket and 60-day Public Comment Period	2013 - March
Close Public Comment	2013 - May
Case Development	
Final Work Plan	2013- August
Issue DCI	2014 – April - June
Data Submission	2016 – April - June
60-day Public Comment Period for Draft Risk Assessments	2017- October-December
Registration Review Decision	
60-day Public Comment Period for Proposed Registration Review Decision	2018 – April - June
Registration Review Decision and Begin Post-Decision Follow-up	2019
Total (years)	6

NEXT STEPS

After the 60-day public comment period closes, the Agency will review and respond to any comments received in a timely manner and then issue a Final Work Plan for the registration review of MSMA.

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Appendix – Additional Areas Considered in MSMA's Registration Review

PUBLIC COMMENTS AND FEEDBACK:

Guidance for Commenters: The areas below highlight topics of special interest to the Agency where your comments, data submissions, or reference to sources of additional information could be of particular use.

Trade Irritants:

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. The Agency will work to harmonize tolerances and international maximum residue limits (MRLs) and may modify tolerance levels to do so, when possible. **Growers and other stakeholders are asked to comment** on any trade irritant issues resulting from lack of MRLs or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

Water Quality:

Total Maximum Daily Loads (TMDL) have been developed for arsenic in several states for several water bodies found in the U.S., based on information provided at EPA's WATERS Expert Query Tool[5]. The TMDL's do not distinguish between the sources of arsenic in water bodies (natural or anthropogenic), so it is not possible to identify water bodies that are impaired by arsenic as a result of pesticidal use, using the available data. Total arsenic (natural and anthropogenic) is identified as a cause of impairment, as defined under section 303(d) of the Clean Water Act, 2,118 times, based on information provided at EPA's WATERS Expert Query Tool. More information on impaired water bodies and TMDLs can be found at EPA's website[6]. **The Agency invites submission of water quality data for this pesticide.** To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process*[7] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

Environmental Justice:

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to MSMA compared to the general population. **Please**

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[5] http://iaspub.epa.gov/pls/waters/f?p=ASKWATERS:EXPERT:0
[6] http://www.epa.gov/owow/tmdl/
[7] http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm

ED_002435_00006468-00012

comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

ENDANGERED SPECIES:

A risk assessment that supports a complete endangered species determination has not been conducted for MSMA. The ecological risk assessment planned during registration review will allow the Agency to determine whether MSMA's use has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Service (the Services), as appropriate.

On January 19, 2011, the Center for Biological Diversity and the Pesticide Action Network North America filed a lawsuit in the United States District Court for the Northern District of California, against the Environmental Protection Agency (EPA) for allegedly failing to undergo consultation with the United States Fish and Wildlife Service and the National Marine Fisheries Service regarding the effects of over 350 pesticides, including inorganic arsenic compounds (to which MSMA can convert in soil and water), on over 200 endangered and threatened species throughout the United States (Center for Biological Diversity, et al. v. EPA, et al., No. C 11-00293 (N.D.Cal.).

ENDOCRINE DISRUPTOR SCREENING PROGRAM:

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for MSMA, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), MSMA is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and

establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. MSMA is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Accordingly, as part of registration review, EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for MSMA. For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website[8].

HUMAN STUDIES:

Occupational and Residential

Past MSMA risk assessments rely in part on data from studies in which adult human subjects were intentionally exposed to a pesticide to determine their dermal and inhalation exposure. Many such studies, involving exposure to many different pesticides, comprise generic pesticide exposure databases such as the Pesticide Handlers Exposure Database (PHED), the Agricultural Reentry Task Force (ARTF) Database, and the Outdoor Residential Exposure Task Force (ORETF) Database. EPA has reviewed all the studies supporting these multi-pesticide generic exposure databases, and has found no clear and convincing evidence that the conduct of any of them was either fundamentally unethical or significantly deficient relative to the ethical standards prevailing at the time the research was conducted. All applicable requirements of EPA's Rule for the Protection of Human Subjects of Research (40 CFR Part 26) have been satisfied, and there is no regulatory barrier to continued reliance on these studies.

[8] http://www.epa.gov/endo/