Docket Number EPA-HQ-OPP-2011-0855
www.regulations.gov

# Paraquat Dichloride Summary Document
# Registration Review: Initial Docket
# December 2011

# Paraquat dichloride Registration Review
# Summary Document: Initial Docket
# December 2011

## Case Number 0262

Approved by: Richard P Keigwin, Jr

Richard P. Keigwin, Jr.
Director
Pesticide Re-evaluation Division

Date: 12/13/2011

## TABLE OF CONTENTS



---

### Please Note

This Preliminary Work Plan and Fact Sheet summarize the Environmental Protection Agency's current position based on the following documents:

1. *EFED Registration Review: Preliminary Problem Formulation for Paraquat Dichloride.* K. Garber. December 12, 2011.

2. *Paraquat Dichloride (Paraquat): Human Health Risk Scoping Document in Support of Registration Review.* B. Daiss. December 6, 2011.

3. *BEAD Chemical Profile for Registration Review: Paraquat Dichloride (Chemical Code 061610).* S. Ratnayake. October 13, 2011.

4. *Paraquat Dichloride Screening Level Usage Analysis (SLUA).* J. Alsadek. February 9, 2011.

5. *Paraquat Dichloride Review of Human Incidents.* Khin Swe Oo. December 12, 2011.

These and other supporting documents for the paraquat dichloride registration review case may be found in the docket HQ-OPP-2011-0855 at http://www.regulations.gov.

# I. PRELIMINARY WORK PLAN – PARAQUAT DICHLORIDE

**Introduction:**

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 at: http://www.epa.gov/oppsrrd1/registration_review/.

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 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 and commit to a final work plan and schedule for the registration review of paraquat dichloride.

Paraquat dichloride is an herbicide used to treat weeds on many crop and non-agricultural (e.g., rights-of-way) use sites. Tolerances are currently established for crop and livestock food commodities. Paraquat dichloride is also applied as a pre-harvest desiccation treatment on some crops including cotton. There are no products registered for homeowner use and no products registered for application to residential areas. Paraquat dichloride products are restricted use pesticides, available for use only by certified applicators or persons under their direct supervision. Paraquat dichloride was first registered in 1964, and the *Reregistration Eligibility Decision (RED) for Paraquat Dichloride* was completed in August 1997. There is a second active ingredient, paraquat dimethyl sulfate salt (PC code 061602) associated with paraquat dichloride's registration review case (0262). However, all paraquat dimethyl sulfate products were cancelled in 1985, and therefore, that active ingredient is not subject to registration review.

**Anticipated Risk Assessment and Data Needs:**

The Agency anticipates the need to require data and to conduct a comprehensive ecological risk assessment, including an endangered species assessment, for all uses of paraquat dichloride. For human health, EPA anticipates the need to require data and to conduct revised dietary and occupational exposure 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 assessment, as well as any changes to the

standard operating procedures (SOPs) or default exposure assumptions. Below is a summary of the issues relevant to the registration review of paraquat dichloride.

*Ecological Risk:*

- The most recent ecological assessment was completed in July 2006 in support of use on a number of new food crops.

- In June 2009, the Agency completed an endangered species assessment evaluating the potential effects of paraquat dichloride on the federally-listed threatened California red-legged frog (*Rana aurora draytonii*) (CRLF) consistent with court orders and settlements, *Center for Biological Diversity* v. *Johnson, et al.,* No. 02-1580 (N.D. Cal., October 20, 2006). This assessment considered all registered uses of paraquat dichloride that are relevant to the state of California. The assessment concluded that paraquat dichloride may affect, and is likely to adversely affect, the CRLF based on the direct effects to the terrestrial-phase CRLF, and indirect effects to the aquatic- and terrestrial-phase CRLF. The Agency initiated formal consultation with the U.S. Fish and Wildlife Service under section 7 of the Endangered Species Act.

- A risk assessment that supports a complete endangered species determination has not been conducted for paraquat dichloride. The ecological risk assessment planned during registration review will allow the Agency to determine whether paraquat dichloride'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 against the EPA in the United States District Court for the Northern District of California 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 paraquat dichloride, 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.).

- An updated comprehensive ecological risk assessment of all registered uses of paraquat dichloride will be conducted during registration review. The new assessment will incorporate the most up-to-date modeling methodologies, updated toxicological endpoints, and data submitted under the anticipated paraquat dichloride registration review data call-in.

- Certain paraquat dichloride labels are unclear with respect to application parameters like the maximum annual numbers of applications or maximum annual application rates. In the absence of clear label information, the Agency must employ conservative assumptions to complete the human health and ecological risk assessments. The Agency encourages clear and consistent label language for the sake of all stakeholders and

encourages the technical registrants to review the product labels for clarity. Please refer to Table 1 of the problem formulation for information on uncertainty on product labels.

- Data gaps exist in the environmental fate and toxicity databases for paraquat dichloride. EPA anticipates requiring the following studies for use in conducting a complete ecological risk assessment, including an endangered species assessment, for the registration review of paraquat dichloride.

  *Environmental Fate:*

  835.4400 – Anaerobic aquatic metabolism

  *Ecotoxicology:*

  850.1025 – Acute toxicity estuarine and marine invertebrate (oyster shell growth)
  850.1035 – Acute toxicity estuarine and marine invertebrate (mysid)
  850.1075 – Acute toxicity estuarine/marine and freshwater fish[1]
  850.1300 – Aquatic invertebrate lifecycle, freshwater
  850.1350 – Aquatic invertebrate lifecycle, saltwater
  850.1400 – Fish early-life stage (freshwater and saltwater)
  850.1735 – Whole sediment: acute freshwater invertebrates
  850.2100 – Avian oral toxicity (passerine species)
  850.4100 – Terrestrial plant toxicity, seedling emergence (Tier II)
  850.4150 – Terrestrial plant toxicity, vegetative vigor (Tier II)
  Non-guideline – Whole sediment: chronic invertebrates, freshwater and marine[2]
  Non-guideline – Acute avian inhalation toxicity

  *Exposure:*
  Non-guideline – Drinking water treatability study

- Please refer to the December 12, 2011 document *EFED Registration Review: Preliminary Problem Formulation for Paraquat Dichloride* in the registration review docket (EPA-HQ-OPP-2011-0855) for a detailed discussion of the anticipated risk assessment and data needs.

*Human Health Risk:*

- The most recent comprehensive human health risk assessment for paraquat dichloride was conducted in July 2006 in support of use on a number of new food crops.

- During registration review, the endpoints, doses, and safety factors used in the most recent human health risk assessments will be revisited based on current policy as well as

[1] Data for three fish species are anticipated to be needed: one warm, freshwater species; one cold, freshwater species; and one estuarine/marine species.
[2] Data for two freshwater species and one estuarine/marine species are anticipated to be needed. The DCI expected to be issued will provide that the studies are to be conducted using Office of Research and Development (ORD) Study Methods, as specified in Section III of this document.

to incorporate any new data received and determined to be adequate.

- The Agency intends to update the acute and chronic dietary (food and drinking water) exposure assessment for paraquat dichloride to include updated drinking water estimated environmental concentrations (EECs), any changes to toxicological endpoints and safety factors, and updates to the percent crop treated values and anticipated residue levels.

- There are no residential uses and no anticipated residential exposures from paraquat dichloride. Therefore, residential handler and post-application exposure assessments are not anticipated to be needed during registration review.

- While there are no registered uses that would result in residential exposure, residential bystander inhalation exposures resulting from off-site transport (e.g., spray drift) may occur as a result of applications of paraquat dichloride. The Agency is in the process of examining its policies and refining the methods used to complete residential exposure assessments. Therefore, the potential need for a bystander inhalation risk assessment will be examined during registration review.

- During registration review, the Agency foresees conducting a reassessment of occupational and aggregate risk, taking into account any relevant changes to toxicological endpoints, safety factors, exposure values, and applicable occupational and residential SOPs.

- The Agency intends to modify tolerance levels as needed, and work to harmonize tolerances/maximum residue limits (MRL), where possible, during registration review.

- The tolerance expression for paraquat dichloride will be reviewed during registration review to ensure that it appropriately covers the metabolites and degradates of paraquat dichloride and that it specifies the residues to be measured for each commodity.

- EPA anticipates the need to require the following data for use in reevaluating and updating the human health toxicity profile for the registration review of paraquat dichloride:

  860.1500 – Crop field trials for corn aspirated grain fractions
  870.3700 – Developmental toxicity – nonrodent
  870.7800 – Immunotoxicity

- Paraquat dichloride is among several agricultural chemicals included in the Agricultural Health Study (AHS). The AHS began in 1993 and is a collaboration of the National Institute of Environmental Health Sciences (NIEHS), the National Cancer Institute (NCI), the EPA, and the National Institute for Occupational Safety and Health (NIOSH). Designed as a large long-term epidemiological study, the AHS collects and analyzes data on the health and work practices of nearly 90,000 farmers and their families in Iowa and North Carolina who enrolled in the study before any disease developed. The study focuses particularly on farmers' exposure to 50 chemicals including many of the most widely used pesticides. As data are collected over a period of years, scientists can

compare overall health outcomes for people who differ in whether they have had exposure to various chemicals. While these comparisons cannot conclusively demonstrate how exposure affects health, they can show some statistical associations. More information on the AHS can be found at: http://aghealth.nci.nih.gov. EPA is monitoring the results of the AHS and will consider this study in the registration review of paraquat dichloride as appropriate.

- Please refer to the December 6, 2011 document *Paraquat Dichloride (Paraquat): Human Health Risk Scoping Document in Support of Registration Review* in the registration review docket (EPA-HQ-OPP-2011-0855) for a detailed discussion of the anticipated risk assessments and data needs.

**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, 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), paraquat dichloride 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. Paraquat dichloride 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 paraquat dichloride. 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: http://www.epa.gov/endo/.

**Timeline:**

EPA has created the following estimated timeline for the completion of paraquat dichloride's registration review.

| Registration Review for Paraquat Dichloride – Projected Registration Review Timeline | |
|---|---|
| **Activities** | **Estimated Date** |
| Opening the Docket | |
| Open Docket and Public Comment Period | 2011 – December |
| Close Public Comment | 2012 – February |
| Case Development | |
| Final Work Plan | 2012 – May |
| Issue DCI | 2013 – Jan. – March |
| Data Submission | 2015 – Jan. – March |
| Open Public Comment Period for Draft Risk Assessments | 2016 – July – Sept. |
| Close Public Comment Period | 2016 – Oct. – Dec. |
| Registration Review Decision | |
| Open Public Comment Period for Proposed Registration Review Decision | 2017 – Jan. – March |
| Close Public Comment Period | 2017 – April – June |
| Registration Review Decision and Begin Post-Decision Follow-up | 2017 |
| Total (years) | 6 |

**Guidance for Commenters:**

The public is invited to comment on EPA's preliminary work plan and rationale. The Agency will carefully consider all comments as well as any additional information or data provided in a timely manner prior to issuing a final work plan for the paraquat dichloride case.

*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. Growers and other stakeholders are asked to comment on any trade irritant issues resulting from lack of Maximum Residue Limits (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:*

Paraquat dichloride is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[3]. In addition, no Total Maximum Daily

[3] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

Loads (TMDL) have been developed for paraquat dichloride[4]. More information on impaired water bodies and TMDLs can be found at the Agency's website[5]. 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*[6] 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 paraquat dichloride compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

*Other Information:*

Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining the risk assessments, including any species-specific ecological determinations. The Agency is interested in obtaining the following information:

1. maximum and typical application rates, and average and maximum amounts of product applied per year, for the following use sites: fallow land; airports; commercial buildings; conservation reserve program land; fencerows; right-of-ways; areas around commercial/industrial buildings, including pumping stations and pipelines; substations; and storage areas
2. confirmation on the following label information
    a. sites of application
    b. formulations
    c. application methods and equipment
    d. maximum application rates
    e. frequency of application, application intervals, and maximum number of applications per season
    f. geographic limitations on use
3. use or potential use distribution (*e.g.*, acreage and geographical distribution of relevant use sites)
4. use history
5. median and 90$^{th}$ percentile reported use rates (lbs ai/1000 sq ft) from usage data – national, state, and county

---

[4] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES

[5] http://www.epa.gov/owow/tmdl/

[6] http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm

6. application timing (date of first application and application intervals) – national, state, and county
7. sub-county use site location data
8. usage/use information for non-agricultural uses
9. directly acquired county-level usage data (not derived from state level data)
    a. maximum reported use rate (lbs ai/acre) from usage data – county
    b. median and 90$^{th}$ percentile number of applications – county
    c. total pounds per year – county
    d. the year the pesticide was last used in the county/sub-county area
    e. the years in which the pesticide was applied in the county/sub-county area
10. typical application interval (days)
11. state or local use restrictions
12. ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
13. monitoring data

**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 paraquat dichloride.

## II. FACT SHEET

**Background Information:**

- Paraquat dichloride registration review case number: 0262. There is a second active ingredient, paraquat dimethyl sulfate salt (PC code 061602) associated with case # 0262. However, all paraquat dimethyl sulfate products were cancelled in 1985 and, therefore, that active ingredient is not subject to registration review.
- Paraquat dichloride PC code: 061601.
- Paraquat dichloride CAS No.: 1910-42-5.
- Paraquat dichloride was first registered for use in the United States in 1964.
- The paraquat dichloride RED was completed in August 1997.
- There are 5 technical registrants, each with one registered technical product. There are 13 end use products. As of October 11, 2011, there are 21 active state-specific Special Local Need (Section 24c) registrations.
- All Section 3 products registered at the time of the RED have been reregistered.
- Tolerances are established for crop and livestock food commodities (40 CFR 180.205).
- Pesticide Re-evaluation Division, Chemical Review Manager: Molly Clayton, *clayton.mollly@epa.gov*
- Registration Division, Product Manager: Kable Davis, *davis.kable@epa.gov*

**Use & Usage Information:** (For additional details on label rates and use sites, refer to *Paraquat Dichloride Screening Level Usage Analysis (SLUA),* dated February 9, 2011 and the *BEAD Chemical Profile for Registration Review: Paraquat dichloride,* dated October 13, 2011, in the registration review docket (HQ-OPP-2011-0855).

- Paraquat dichloride is an herbicide primarily used to treat weeds on many crops prior to planting. Also, it can be applied as a band, spot, or directed treatment after crop emergence. In addition, it is applied as a pre-harvest desiccation treatment on some crops, including cotton, and is registered for use on a variety of nonagricultural use sites.

- As described on page 10 of this document, the Agency requests the following information to inform the upcoming registration review human health and ecological risk assessments: maximum and typical application rates; and average and maximum amounts of product applied per year for fallow land, airports, commercial buildings, conservation reserve program land, fencerows, right-of-ways, areas around commercial/industrial buildings, including pumping stations and pipelines, substations, and storage areas.

- In 1978, due to high acute toxicity to animals and humans through inadvertent exposure, paraquat dichloride was classified as "restricted use." All paraquat dichloride products are to be used only by certified applicators or persons under their direct supervision.

- Paraquat dichloride is formulated as flowable and emulsifiable concentrates only.

- There are no products registered for homeowner use and no products registered for

application to residential areas.

- From 1998-2010, the annual total agricultural usage averaged approximately 3 million pounds active ingredient for 7 million treated acres.

- From 1998-2010, the crops with most significant usage of paraquat dichloride are caneberries (70% of crops were treated with paraquat dichloride), artichokes (40%), pistachios (40%), and almonds (35%).

**Pending Actions:**

There is a pending action (petition # 0E7748) for the establishment of tolerances on subtropical and tropical fruit trees. The Agency plans to make a decision with regards to these tolerances by August 7, 2012.

**Ecological Risk Assessment Status:**

Please refer to the *EFED Registration Review: Preliminary Problem Formulation for Paraquat Dichloride*, dated December 12, 2011 for a detailed discussion of the key findings of the most recent ecological risk assessments. A summary follows:

- The most recent ecological assessment was completed in July 2006 in support of use on a number of new food crops.

- The primary route of environmental dissipation of paraquat is adsorption to soil clay particles. It was not observed to desorb from these particles in a laboratory test. Paraquat does not hydrolyze and is photodegraded very slowly in aqueous solutions. It is resistant to microbial degradation under aerobic and anaerobic conditions.

- Risk conclusions in the 2006 assessment were similar to previous conclusions, and indicated risks of concern for plants, aquatic invertebrates, mammals, birds, terrestrial-phase amphibians, and reptiles. It is practically nontoxic to honeybees.

- In June 2009, the Agency completed an endangered species assessment evaluating the potential effects of paraquat dichloride on the Federally-listed threatened California red-legged frog (*Rana aurora draytonii*) (CRLF). This assessment considered all registered uses of paraquat dichloride that are relevant to the state of California. The assessment concluded that paraquat dichloride may affect, and is likely to adversely affect, the CRLF based on the direct effects to the terrestrial-phase CRLF, and indirect effects to the aquatic- and terrestrial-phase CRLF. Indirect effects are specifically related to declines in prey (algae, amphibians, mammals) and habitat of the frog.

- Based on the environmental and human health risk estimates from the RED, the Agency specified risk reduction measures to mitigate human health and ecological risk concerns. These included lowering the maximum application rate to 1 pound cation/acre, which is equivalent to 1.417 pounds active ingredient per acre.

**Human Health Risk Assessment Status:**

Please refer to *Paraquat Dichloride (Paraquat): Human Health Risk Scoping Document in Support of Registration Review,* dated December 6, 2011, for a detailed discussion of the key findings of the most recent human health risk assessment. A summary follows:

*Hazard Characterization*:

- The most recent comprehensive human health risk assessment was completed in 2006.

- Subchronic and chronic toxicity studies in mice, rats and dogs indicate that the lung is the principal target organ for repeated exposure to paraquat. Paraquat is highly acutely toxic via inhalation, dermal and oral routes of exposure.

- In the 2006 assessment, an uncertainty factor of 100x (10x for interspecies extrapolation and 10x for intraspecies variation) was applied for the dermal and inhalation routes of exposure. The FQPA safety factor was reduced to 1x based on available toxicity studies. However, a database uncertainty factor ($UF_{DB}$) of 3x was applied to the subpopulation females 13-49 due to lack of an acceptable developmental study in a non-rodent species.

*Dietary (Food and Drinking Water)*:

- In the 2006 assessment, acute and chronic dietary and drinking water assessments indicated that estimated risks were not of concern for the general U.S. population and all population subgroups.

*Residential (Non-occupational):*

- Because there are no paraquat products registered for homeowner use and there are no products registered for application to residential areas, a residential assessment has not been conducted.

*Aggregate:*

- Since there are no residential uses of paraquat, acute and chronic aggregate risks are equivalent to estimated acute and chronic dietary (food and water) risks respectively. The Agency concluded that acute and chronic dietary risks for paraquat were not of concern in the 2006 risk assessment

*Occupational:*

- In the 2006 assessment, occupational risk estimates were not of concern for any exposure scenario.

*Human Studies:*

- Previous occupational risk assessments for paraquat dichloride relied in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. Dermal absorption was examined in a series of special studies in which test material was applied dermally to adult male volunteers. These studies required a review of their ethical conduct and have received the appropriate review by the Human Studies Review Board (HSRB).

- Past paraquat dichloride risk assessments have relied in part on a chemical-specific biomonitoring study which may have involved intentional exposure to paraquat dichloride. In the course of registration review, EPA will reconsider this study, as well as any other research involving intentional exposure of human subjects to paraquat dichloride brought to its attention. If EPA decides to rely on any of these studies, EPA will ensure that all applicable regulatory requirements are met, including but not limited to the requirements for EPA ethics review and Human Studies Review Board review of certain research involving intentional exposure of human subjects.

- Past paraquat dichloride 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) 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.

*Cumulative:*

- EPA has not yet determined whether or not paraquat dichloride shares a common mechanism of toxicity with other chemical substances. If the Agency determines that new information on paraquat dichloride is available that could potentially affect a cumulative risk assessment and result in a risk of concern, the Agency will revisit the need for a cumulative assessment.

**Incidents:**

- A review of the Ecological Incident Information System (EIIS), the 'Aggregate Incident Reports' (AIR) database, and the Avian Monitoring Information System (AIMS) for ecological incidents involving paraquat dichloride was completed on August 31, 2011. Thirty incidents were reported in EIIS. Twenty-one of the incidents in EIIS were damage to plants, typically from post-application drift to crops. Six of the incidents in EIIS involved death to varying numbers of fish (numbers ranging from unknown to 200), and three incidents involved the death of 5 or fewer birds. The aggregate incident database

included 82 minor plant incidents, 4 minor fish and wildlife incidents and 3 "other" non-target incidents that were reported between 1995 and 2010. Two incidents involving an unknown number of birds were identified in the AIMS database. One of the incidents was also reported in EIIS, and the other involved another pesticide (carbofuran). For all incidents, the degree of certainty ranged between possible and probable.

- An updated human health incident report was conducted for paraquat dichloride for registration review. From January 1, 2006 to June 8, 2011, there were 119 incidents involving paraquat dichloride in the Main Incident Data System (IDS). Seventy-three cases involved products with more than one active ingredient (i.e., pesticides other than and including paraquat dichloride), and 46 cases were reported for products in which the single active ingredient was paraquat dichloride. There was one human death associated with ingestion of paraquat dichloride; it was unclear whether the ingestion was intentional or accidental. Nine of the incidents were classified as major, and 36 were classified as moderate. Of the major incidents, 30% of cases were intentional ingestion, 30% were accidental ingestion, 20% were ingestion of unknown intention, and 20% were cases of accidental dermal exposure. In addition, epidemiologic findings from the Agricultural Health Study (AHS) investigated a possible link of paraquat dichloride exposure in the etiology of Parkinson's disease. The Agency will consider these AHS findings and any other literature pertinent to paraquat exposure and toxicity as part of the registration review evaluation for paraquat dichloride.

**Tolerances and International Harmonization:**

- U.S. tolerances and international MRLs for paraquat dichloride are not compatible for a significant number of commodities for which tolerances have been established by both entities. U.S. and Canadian tolerances are compatible for all jointly registered commodities. A summary of U.S. tolerances and international MRLs, including commodities for which U.S. tolerances differ from Codex MRLs, is included in the *Paraquat Dichloride (Paraquat): Human Health Risk Scoping Document in Support of Registration Review*, dated December 6, 2011.

**Data Call-In Status:**

- Six generic data call-ins (GDCI-061601-16121, GDCI-061601-16392, GDCI-061601-16575, GDCI-061601-16831, GDCI-061601-17753) were issued between June 1987 and August 1997. These data requirements have been fulfilled.

**Labels:**

- Registration numbers and labels for paraquat dichloride products can be obtained from the Pesticide Product Label System (PPLS) website[7].

[7] http://oaspub.epa.gov/pestlabl/ppls.home

## III. SUMMARY OF DATA GAPS – PARAQUAT DICHLORIDE

The table below summarizes all anticipated data needs for paraquat dichloride.

| Guideline Number | Anticipated Data Need | Test Material | Estimated Timeframe (Months from receipt of DCI) |
|---|---|---|---|
| **Environmental Fate** | | | |
| 835.4400 | Anaerobic aquatic metabolism | TGAI | 24 |
| **Environmental Effects** | | | |
| 850.1025 | Acute toxicity estuarine and marine organisms (oyster shell growth) | TGAI | 12 |
| 850.1035 | Acute toxicity estuarine and marine organisms (mysid) | TGAI | 12 |
| 850.1075 | Acute toxicity estuarine and marine organisms (one warm freshwater species, one cold freshwater species, and one estuarine/marine species) | TGAI | 12 |
| 850.1300 | Aquatic invertebrate lifecycle, freshwater | TGAI | 12 |
| 850.1350 | Aquatic invertebrate lifecycle, saltwater | TGAI | 12 |
| 850.1400 | Fish early-live stage, freshwater and saltwater | TGAI | 12 |
| 850.1735 | Whole sediment: acute freshwater invertebrates | TGAI | 12 |
| 850.2100 | Avian oral toxicity (passerine species) | TGAI | 12 |
| 850.4100 | Terrestrial plant toxicity, seedling emergence, Tier II[8] | TEP | 12 |
| 850.4150 | Terrestrial plant toxicity, vegetative vigor, Tier II[8] | TEP | 12 |
| Non-guideline | ORD study method EPA 600/R-099-064: chronic freshwater sediment testing flowthrough (Hyalella azteca) | TGAI | 24 |
| Non-guideline | ORD study method EPA 600/R-099-064: chronic freshwater sediment testing flowthrough (Chironomus dilutus or C. tentans) | TGAI | 24 |
| Non-guideline | ORD study method EPA 6001R-0l/020: chronic estuarine/marine sediment testing flowthrough (Leptocheirus plumulosus) | TGAI | 24 |
| Non-guideline | Acute avian inhalation study | TGAI | 24 |
| **Exposure** | | | |
| Non-guideline | Drinking water treatability study | TGAI | 8 |
| 860.1500 | Crop field trials for corn aspirated grain fractions | TEP | 24 |
| **Human Health Effects** | | | |
| 870.3700 | Developmental toxicity, nonrodent | TGAI | 24 |

[8] The DCI expected to be issued will provide that a Tier I plant study may be conducted in lieu of a Tier II study with the understanding that any adverse effects observed by the Tier I study would necessitate conduct and submission of a Tier II study as well.