



United States
Environmental Protection
Agency (7508C)

Office of Prevention, Pesticides
and Toxic Substances

July 7, 2005

Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Procymidone



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Reader:

This is the Environmental Protection Agency's (hereafter referred to as EPA or the Agency) "Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision for Procymidone," which was approved on July 6, 2005. This document is also known as a Tolerance Reassessment Decision, or TRED. A Notice of Availability of this tolerance reassessment decision will be published shortly.

The Federal Food, Drug and Cosmetic Act (FFDCA), as amended by FQPA, requires EPA to reassess all the tolerances for registered chemicals in effect on or before the enactment of the FQPA on August 3, 1996. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. Once a safety finding has been made, the tolerances are considered reassessed. Existing tolerances and exemptions associated with procymidone must be reassessed in accordance with FFDCA, as amended by FQPA.

Procymidone is a fungicide used to treat wine grapes outside of the United States. A tolerance of 5 ppm for wine grapes has been established, with no U.S. registrations, to permit the import of wine produced from procymidone treated grapes. Currently, procymidone exposures to the U.S. general population exist only through drinking imported wine made from procymidone treated grapes. Since there are no registered uses of procymidone in the U.S., no occupational, residential, or drinking water exposures are expected.

The Agency has completed the human health risk assessment for procymidone. These findings are presented fully in the human health risk assessment document, "*Procymidone: HED Chapter of the Tolerance Reassessment Eligibility Decision Document*," dated June 13, 2005. The procymidone toxicological database is adequate for hazard characterization and sufficient data are available to assess potential susceptibility to the young. Therefore, the FQPA Safety Factor (SF) was reduced to 1X.

Acute and cancer dietary assessments were performed for procymidone. A chronic dietary

assessment was not performed since the same NOAEL and endpoint (developmental effect, NOAEL = 3.5 mg/kg/day) were chosen for both chronic and acute assessments. The dietary exposure analysis for food resulted in risk estimates below the Agency's level of concern. A Tier I acute dietary assessment was performed for procymidone. At the 95th percentile, acute dietary risk were 1.7% of the acute Population Adjusted Dose (aPAD) for females 13-49. The Agency classified procymidone as a probable human carcinogen. Cancer risk was estimated to be 1.8×10^{-6} . Conservative assumptions were used in conducting the cancer analysis. Thus, actual exposure is likely to be substantially lower than the estimated exposure and consequently not of concern.

3,5-Dichloroaniline (3,5-DCA) is a common metabolite to iprodione, vinclozolin, and procymidone. The 3,5-DCA metabolite was not detected in grapes, but occurs during fermentation. Based on modeling from drinking water residues of 3,5-DCA, cancer risk estimates from iprodione and vinclozolin exceeded the Agency's level of concern. Mitigation and monitoring were imposed for iprodione and vinclozolin to deal with these exceedences.

A cancer assessment was performed for 3,5-DCA as a result of all three chemical uses in food and wine only. The aggregate carcinogenic risk estimate for consumption of food and wine containing residues of 3,5-DCA as a result of use of iprodione, vinclozolin, and procymidone is 1.3×10^{-6} . To obtain the carcinogenic risk estimate for 3,5-DCA, the established Q_1^* for p-chloroaniline (PCA) was used as a surrogate Q_1^* in this assessment because of the structural similarities between 3,5-DCA and PCA. EPA believes that the use of the PCA Q_1^* represents a reasonable risk estimate.

There are no data gaps for procymidone. Based on the human health assessment, risks associated with procymidone are considered to be minimal in the United States due to its low acute toxicity and its low dietary exposure. Therefore, no mitigation measures are needed, and the current tolerance for wine grapes at 40 CFR 180.455 for residues of procymidone is now considered reassessed under section 408(q) of the FFDCA.

FQPA requires that EPA consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency considers other substances because low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect, as would a higher level of exposure to any of the substances individually.

EPA has not made a common mechanism of toxicity finding and therefore, has not assumed that procymidone has a common mechanism of toxicity with other substances for the purposes of this tolerance action. However, procymidone is structurally related to vinclozolin and iprodione, and the metabolite 3,5-DCA is produced by each of these chemicals.

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances "may have an effect in humans that is similar to endocrine effects." Procymidone is known to interfere with the endocrine system related to its anti-androgenic activity ultimately resulting in reproductive effects. In several studies, a number of testicular effects were observed at one or more dose levels in the developmental, multigeneration, and chronic toxicity studies in rats. When additional appropriate screening and/or testing protocols currently being

considered under the Agency's Endocrine Disruptor Screening Program (EDSP) have been developed, procymidone may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

This document summarizes the Agency's decision on the tolerance reassessment for procymidone. Please contact Demson Fuller of my staff with any questions regarding this decision. He may be reached by phone at (703-308-8062) or via e-mail at fuller.demson@epa.gov.

Sincerely,

Debra Edwards, Ph.D.
Director
Special Review and Reregistration Division