50 mg/kg. The NOEL for maternal toxicity was 10 mg/kg (equivocal). The LEL was 50 mg/kg based on decreased body weight gain during dosing. Developmental effects were also evaluated. Hydrocephalus internus was observed in 1 fetus at each treatment level. Therefore, the NOEL for developmental toxicity was set at less than 2 mg/kg, and the LEL was 2 mg/kg. The incidence was 0.85, 0.83, and 0.93 for the low-, mid-, and high-dose fetuses and 0.08 for the historical control.

9. A New Zealand white rabbit developmental toxicity study in which cyproconazole (94.8% purity) was administered by gavage to 18 inseminated New Zealand White rabbits once daily on days 6 through 18 of gestation at dose levels of 2, 10, or 50 mg/kg. The NOEL for maternal toxicity was 10 mg/kg, and the LEL was 50 mg/ kg based on decreased body weight gain. There was also evidence of developmental toxicity. The NOEL for developmental toxicity was 2 mg/kg, and the LEL was 10 mg/kg based on the increased incidence of malformed fetuses and litters with malformed fetuses.

10. A rat two-generation reproduction study in which technical cyproconazole (95.6% purity) was administered to 26 male and 26 female Fo and F1 KFM-Wistar rats per group for 10 and 12 weeks, respectively, during the premating period via the diet at 0, 4, 20, or 120 ppm. Treatment of males continued for 3 weeks after termination of mating and females were treated until necropsy (post-weaning). The systemic NOEL for parental toxicity was set at 20 ppm (1.7 mg/kg) based on liver effects at 10.6 mg/ kg/day. For reproductive toxicity, the NOEL was set at 4 ppm (0.4 mg/kg) and the LEL at 20 ppm (1.7 mg/kg) based on increased gestation length in the F<sub>0</sub> dams and decreased F<sub>1</sub> litter sizes.

Several mutagenicity studies. Mutagenicity potential of cyproconazole was tested in several studies considered acceptable by the Agency. Since the results of two chromosomal aberration assays indicated the cyproconazole is clastogenic, additional mutagenicity data were requested to address an identified heritable risk concern. For the potential to induce chromosome aberrations in CHO cells, cyproconazole was positive under nonactivated and activated conditions, thus supporting the evidence that cyproconazole is clastogenic in this test system. Cyproconazole was negative in Salmonella, mouse micronucleus, and SHE/cell transformation assays. A dominant-lethal assay in rats was submitted and was negative. Based on

this evidence, the concern for a possible heritable effect was not pursued.

12. Metabolism/pharmacokinetics studies. Cyproconazole was shown to be extensively metabolized in the rat. Unchanged cyproconazole and 13 metabolites were isolated and identified, and 35 metabolites were detected in the excreta. Excretion was relatively rapid with the majority of the radioactivity appearing in the feces as a result of biliary elimination. Residues were found in renal fat, adrenals, kidney and liver, although no significant tissue radioactivity was observed at 168 hours post-dose.

The reference dose (RfD) used in the dietary exposure analysis was 0.01 mg/ kg bwt/day based on a NOEL of 30.0 ppm (1.00 mg/kg bwt/day) from a 1-year dog feeding study with an uncertainty factor of 100 that demonstrated hepatotoxicity and organ weight changes observed at 3.2 mg/kg/day. The theoretical maximum residue contribution (TMRC) for the general population is 0.000002 mg/kg/day and for females, 20 years old and older, the TMRC is 0.000003 mg/kg/day. The anticipated residue contributions (ARC) as percentages of the RfD are 0.018 and 0.028% for the general population and females 20 years old or older, respectively. The chronic analysis for cyproconazole is not a worst-case estimate of dietary exposure, with all residues at anticipated levels and 100% of the commodities assumed to be treated with cyproconazole. Based on the risk estimates calculated in this analysis, it appears that chronic dietary risk from the use recommended is not of concern.

The upper-bound cancer risk, based on a  $Q_1^*$  of 0.30 (mg/kg/day)<sup>-1</sup>, was calculated to be 5.3 x  $10^{-7}$ , contributed through the proposed use of cyproconazole in the production of imported coffee beans. The carcinogenic analysis demonstrates that, using the proposed anticipated residues and without percent crop treated information incorporated into the analysis, the use on coffee does not result in a risk estimate exceeding the Agency's value for negligible cancer risk of  $10^{-6}$ .

The nature of the residue in coffee is not fully understood. A metabolism study in coffee, using triazole-labeled cyproconazole, was submitted and was acceptable. Cyproconazole per se was the primary component of the residue. A metabolism study in wheat is being conducted to determine the fate of the phenyl portion of cyproconazole in plants. Preliminary results of the study have been submitted. It is the Agency's conclusion that the results of this study

will not significantly alter the risk evaluation for cyproconazole and, therefore, establishing a time-limited tolerance for coffee beans would not pose any significant dietary risk to the public during the timeframe involved in completing and reviewing the wheat metabolism data on this chemical.

Adequate analytical methodology is available for enforcement. However, additional data are required to demonstrate that residues of several other pesticides registered for use on coffee do not interfere with the method. Prior to publication in the Pesticide Analytical Manual, Vol. II, the enforcement methodology is being made available in the interim to anyone who is interested in pesticide enforcement when requested from: Calvin Furlow, Public Response and Program Resource Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460 Office location and telephone number: Rm. 1130A, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202, (703)-305-5937.

The pesticide is considered useful for the purpose for which the tolerance is sought. Based on the information and data considered, the Agency has determined that the tolerance established by amending 40 CFR part 180 will protect the public health. Therefore, the tolerances are established as set forth below. By way of public reminder, this notice also reiterates the registrant's responsibility under section 6(a)(2) of FIFRA, to submit additional factual information regarding adverse effects on the environment and to human health by these pesticides.

Any person who has registered or submitted an application for registration of a pesticide, under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended, which contains any of the ingredients listed herein, may request within 30 days after publication of this notice in the **Federal Register** that this rulemaking proposal be referred to an Advisory Committee in accordance with section 408(e) of the FFDCA.

Interested persons are invited to submit written comments on the proposed regulation. Comments must bear a notation indicating the document control number, [PP 0E3875/P623]. All written comments filed in response to this petition will be available in the Public Response and Program Resources Branch, at the address given above from 8 a.m. to 4:30 p.m., Monday through Friday, except legal holidays.

A record has been established for this rulemaking under docket number [PP