additional data are necessary to more completely define the mechanism of clofentezine's thyroid tumor induction in terms of the criteria listed in the above document. Based on the rat feeding/ carcinogenicity study, the Agency has classified clofentezine as a possible human carcinogen (Group C). The qualitative designation "C" refer to EPA's weight-of-evidence classification. The classification is based on the Agency's "Guidelines for Carcinogenic Risk Assessment," published in the Federal Register of September 25, 1996 (51 FR 33992). The Agency believes a quantitative risk assessment based on the thyroid incidence is not approprate for the following reasons:

1. The increase tumor incidence was marginally increased above the control incidence only at the highest dose tested (20 mg/kg/day) in the chronic feeding study.

2. The increased incidence was observed only in male rats.

3. The thyroid tumor incidence in the chronic feeding study's highest dose group (20 percent) was slightly greater than the historical range provided by limited control group data (7.5 to 15 percent) from two other studies.

4. The additional thyroid function studies suggest the possibility of an indirect mechanism for follicular cell tumor induction that may be associated with clofentezine's liver toxicity.

5. The mouse was negative for carcinogency effects at all dose levels, i.e., 50, 500, 5,000 ppm (equivalent to 7.5, 75, 750 mg/kg/day, respectively).

6. There are no close structural analogs with carcinogenic concerns identified.

7. Clofentezine is not mutagenic in several acceptable studies.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Science Advisory Panel (SAP) also reviewed the weight-of-evidence consideration and classification of the carcinogenic potential of clofentezine. The SAP review included the additional thyroid studies submitted by Nor-Am that were available at that time. The SAP concluded that thyroid tumors in male rats from the chronic feeding/ carcinogenicity study with clofentezine did not provide adequate evidence of a potential carcinogenic hazard to humans and that the carcinogenic potential of clofentezine belongs to Group D (not classifiable as a human carcinogen).

The Panel's interpretation was based on observed increases in thyroid stimulation hormone (TSH) levels and the incidence of thyroid follicular cell hyperplasia which may be responses to decreases in blood levels of the

circulating thyroid hormones (triiodothyroxine (T<sub>3</sub>) and tetraiodothyroxine  $(T_4)$  observed in clofentezine-treated rats. This sequence of reduced circulating thyroid hormones and increased TSH levels and follicular cell hyperplasia is known to lead to thyroid tumors in rats, and the Panel noted, "Exposure to agents that cause this sequence in rats has not resulted in increased TSH, hyperplasia, and thyroid tumors in humans." Therefore, the Panel concluded that there was inadequate data for suggesting human carcinogenicity or a quantitative risk assessment.

Nor-Am has since submitted additional thyroid studies intended to show the mechanism of clofentezine's thyroid tumor induction. The Agency has reviewed these data, but as previously stated, the Agency continues to believe that additional data are needed to more completely define the mechanism of clofentezine's thyroid tumor induction and that the available data are not sufficient to change the classification of clofentezine from Category "C" to Category "D." However, the Agency does agree with the SAP that a quantitative risk assessment is not appropriate.

The reference dose (RfD), based on the 1-year dog feeding/carcinogenic study with a NOEL of 1.25 mg/kg/bwt and 100-fold uncertainity factor, is calculated to be 0.013 mg/kg/bwt. The theoretical maximum residue contribution (TMRC) from published uses is 0.000591 mg/kg/bwt/day. This represents 4.54 percent of the RfD. The proposed tolerance contributes .000231 mg/kg/bwt/day. This represents 1.78 precent of the RfD. Dietary exposure from the existing uses and proposed uses will not exceed the reference dose for any subpopulation (including infants and children) based on the information available from EPA's Dietary Risk **Evaluation System.** 

The nature of the residue is understood. An adequate analytical method, high-performance liquid chromatography (HPLC), is available for enforcement.

Also, in an editorial amendment to the clofentezine tolerances in 40 CFR 180.446, EPA is removing the sole entry in paragraph (a), for pears, and moving it to the table in paragraph (b). Paragraph (a) is redundant and is being removed and designated as "reserved."

There are currently no actions pending against the continued registration of this chemical.

This pesticide is considered useful for the purposes for which the tolerances are sought and capable of achieving the intended physical or technical effect. Based on the information and data considered, the Agency has determined that the tolerances established by amending 40 CFR part 180 will protect the public health. Therefore, the tolerance is established as set forth below.

Any person adversely affected by this regulation may, within 30 days after publication of this document in the **Federal Register**, file written objections to the regulation and may also request a hearing on those objections. Objections and hearing requests must be filed with the Hearing Clerk, at the address given above (40 CFR 178.20). A copy of the objections and/or hearing requests filed with the Hearing Clerk should be submitted to the OPP docket for this rulemaking. The objections submitted must specify the provisions of the regulation deemed objectionable and the grounds for the objections (40 CFR 178.25). Each objection must be accompanied by the fee prescribed by 40 CFR 180.33(i). If a hearing is requested, the objections must include a statement of the factual issue(s) on which a hearing is requested, the requestor's contentions on such issues, and a summary of any evidence relied upon by the objector (40 CFR 178.27). A request for a hearing will be granted if the Administrator determines that the material submitted shows the following: There is genuine and substantial issue of fact; there is a reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested claims or facts to the contrary; and resolution of the factual issue(s) in the manner sought by the requestor would be adequate to justify the action requested (40 CFR 178.32)

Under Executive Order 12866 (58 FR 51735, October 4, 1993), the Agency must determine whether the regulatory action is "significant" and therefore subject to al  $\ensuremath{\bar{l}}$  the requirements of the Executive Order (i.e., Regulatory Impact Analysis, review by the Office of Management and Budget (OMB)). Under section 3(f), the order defines "significant" as those actions likely to lead to a rule (1) having an annual effect on the economy of \$100 million or more, or adversely and materially affecting a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local or tribal governments or communities (also known as "economically significant"); (2) creating serious inconsistency or otherwise interfering with an action taken or planned by another agency; (3) materially altering the budgetary