male SD rats were administered the chemical by gavage over a period of 18 weeks (low dose: 0.25 ml/kg; high dose 0.50 ml/kg). Electrophysiological changes observed at 18 weeks in all test animals included a significant reduction in nerve conduction velocity and an important increase of both relative and absolute refractory period. Light and electron microscopic examination of sciatic nerve from all test animals showed the presence of degenerating myelin sheaths accompanied by axonal swelling. An advanced stage of degeneration was indicated by the presence of lamellated electron dense inclusions in unmyelinated nerve fibers.

"Tri-n-butyl phosphate was administered by gavage to male and female Sprague-Dawley rats for 14 consecutive days (low dose: 0.14 ml/kg, high dose: 0.42 ml/kg). Effects of this chemical were investigated at the end of the feeding period. Histopathological examination of the testes (high-dose group) showed the presence of microscopic degenerative changes in the seminiferous tubules. No other abnormal microscopic changes were observed."

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EPA STUDYING FOOD ADDITIVE TOLERANCE-DELANEY CLAUSE LINK

Holding its ground on setting food additive tolerances for residues of dicamba under the constituents policy, EPA Dec. 5 indicated it is weighing the entire relationship of food additive tolerances for pesticides with the Delaney anti-cancer clause.

The agency said it "is particularly concerned about situations where new data demonstrated for the first time a carcinogenic potential for pesticides for which food additive regulations have already been established." EPA said it will "address this subject in a Federal Register notice that will discuss the various options for dealing with such situations and will request public comment on these options."

Responding to questions raised by Rep. Brown (D-Calif.) about the constituents policy - - under which a non-carcinogenic additive can be approved although it contains a carcinogenic constituent - - EPA said the new policy would not be used for "deliberately added active or inert ingredients, or metabolites thereof." The Federal Register document stated that the agency would only consider applying the constituents policy for "impurities arising from the manufacture of the pesticide (residual reactants, intermediates, and products of side reactions and chemical degradates)."

The discussion of the constituents policy came with the rejection of a petition from the Natural Resources Defense Council (NRDC) that food additive and feed additive tolerances set for residues of dicamba based on the constituents policy be stayed. EPA denied the petition.

The agency had set food and feed additive tolerances of 2.0 p.p.m. in sugarcane molasses for residues of the herbicide - - 3,6-dichloro-o-anisic acid and its metabolite 3,6-dichloro-5-hydroxy-o-anisic acid (See March 23, 1983, Page 9). The tolerances had been petitioned by Velsicol. The constituents policy was used because of the dimethyl-N-nitrosamine (DMNA) impurity.

After NRDC attacked the tolerances, EPA reaffirmed its position, but permitted more time for the filing of objections. Last week, the agency said the tolerances satisfy "criteria set forth in the Federal Food, Drug & Cosmetic Act."

EPA Declines to Adopt De Minimis Policy

Velsicol submitted comments suggesting that, in addition to the constituents policy, EPA could apply a de minimis policy, urging that this could provide an alternative basis for

e dicamba tolerances. However, the agency said it "chooses not to decide at this time hether a 'de minimis' rationale . . . is available under §409 of the Federal FD&C Act cases involving the proper use of pesticides on food crops, since that decision is unecessary to resolve the matter at hand."

n response to NRDC's request that it discuss the applicability of the Delaney clause, EPA aid its earlier documents "more than adequately delineate the agency's rationale . . ." The agency noted that it had relied on the Food and Drug Administration's rationale for using the constituents policy in approving a color additive, adding that FDA's policy was upheld in court in a case involving another color additive.

Rep. Brown, who is chairman of the House Agriculture Committee's subcomittee on Department Operations, Research and Foreign Agriculture, urged EPA to review all aspects of the constituents policy. EPA replied that it "will consider using this rationale in issuing a food additive regulation only where the potential risk from the impurity is extremely low."

Discussing EPA's risk estimate, Velsicol said the higher level of DMNA detected in the dimethylamine salt formulation of dicamba registered for sugarcane use is 0.445 p.p.m., much lower than the 3.0 p.p.m. value used by the agency. With the lower figure, the company said, the worst-case lifetime risk would be $4.66X10^{-10}$.

EPA replied that its "use of the 3 p.p.m. value in the risk assessment was correct," explaining that the highest value of DMNA in the Velsicol formulation is 0.445 p.p.m., but that a sample of another dimethylamine dicamba product was reported containing 2.98 p.p.m. DMNA. "Since dimethylamine is considered to be the source of DMNA in these dicamba products, it is reasonable to assume that the product registered for sugarcane use could contain as much as 3 p.p.m. DMNA," the agency said.

Noting that Velsicol supported its position that DMNA is extremely volatile and breaks down in the presence of ultraviolet light, EPA agreed "that the actual concentration of DMNA in sugarcane is likely to be lower than the calculated value of 0.75 p.p.t. because of the volatility and light sensitivity of this compound." However, the agency said it "does not believe that a modification of the 0.75 p.p.t. number is justifiable because of the other factors involved, such as differences between DMNA and dicamba in their uptake by plants and their biodegradability in the soil."

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ERANCES SET FOR IPRODIONE, DIAZINON, MEVINPHOS

EPA Dec. 5 established tolerances for three pesticides, renewed a temporary tolerance for a pesticide, broadened the exemption of an adjuvant from tolerance requirements and proposed exemptions for two other adjuvants, and noted 6 petitions covering 4 pesticides, the amendment of 5 pending tolerance petitions, and withdrawal of 1 petition.

Tolerances were set for residues of iprodion -- 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine-carboxamide and its metabolites 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide -- of 60.0 p.p.m. in or on grapes. A temporary tolerance for grapes of 20 p.p.m. would have expired Dec. 31, 1984. Tolerances also were for residues of the fungicide and its non-hydroxylated metabolites of 0.8 p.p.m. in eggs; 0.4 p.p.m. in poultry meat and meat byproducts (except liver and kidney); 2.0 p.p.m. in poultry fat; and 3.0 p.p.m. in poultry liver.

At the same time, tolerances for residues of iprodione and its non-hydroxylated metabolites in meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep of 0.1 p.p.m. were changed to 0.4 p.p.m. in meat, fat and meat byproducts (except liver and kidney) of cattle, goats, hogs, horses and sheep; and 3.0 p.p.m. in kidney and liver of cattle, goats, hogs, horses, and sheep.