List A Rereg
10-31-95

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 31 1995

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **ACEPHATE.** List A. Valent. CBRS Comments on Proposed Protocol for Pyrolysis Study. Shaughnessy No. 103301; DP Barcode: D210615; CBRS No. 16078; MRID No.: NO MRID; Rereg. Case No. 0042; PRAT Case No. 819371.

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Background

On 3/2/94 a DCI was issued to Valent USA Corporation. A 90-Day Response dated on 5/31/94 was received by the Agency which stated Valent's intent to submit a Tobacco Pyrolysis Protocol to the Agency for review prior to initiating the study on acephate.

Acephate is an organophosphate insecticide. Tolerances are established for combined residues of acephate (O,S-dimethyl acetylphosphoramidothioate) and its cholinesterase-inhibiting metabolite methamidophos (O,S-dimethyl phosphoramidothioate) in or on numerous commodities, including: cottonseed, 2 ppm; soybeans, 1 ppm; cattle, goats, hogs, horses, poultry, and sheep (fat, meat, and MBYP), milk and eggs, 0.1 ppm [40 CFR §180.108(a)]; and soybean meal, 4 ppm; cottonseed meal, 8 ppm; and cottonseed hulls, 4 ppm [40 CFR §186.100]. CBRS has determined that a food additive tolerance for soybean hulls (8X concentration) is required (Acephate Registration Standard Update 8/8/91).

The available data indicate that combined residues of acephate and methamidophos will exceed 0.1 ppm in or on green and cured tobacco leaves (Acephate Reregistration Standard Update 1/29/91). Subdivision "O" has designated that cigarette pyrolysis studies are required when residues exceed 0.1 ppm in cured tobacco. The pyrolysis products of acephate must be characterized and the level of the residue in smoke must be quantified.

Recommendations/Conclusion:

The Pyrolysis protocol is acceptable with the recommended modifications discussed below.

Detailed Considerations

Protocol Review for project no. PRTL No. 904, VP-10987.

According to the Pesticide Assessment Guidelines, the use of a pesticide on tobacco does not require a tolerance or exemption from the requirements to obtain a tolerance, but does require the submission of data needed to assess the exposure of man to the residue remaining at the time of use of the tobacco. The data required include a residue profile for the tobacco and its smoke. This residue profile must include the active ingredient and all significant plant metabolites of the active ingredient, translocated degradation products, and photodegradation products. Radioisotopic techniques will normally be required to identify the significant components of the residue.

The registrant has submitted a protocol for review. The stated objectives of the proposed study are to determine the distribution of [^{14}C] pyrolysis products in main stream cigarette smoke using cigarettes made from laboratory-fortified tobacco and to identify the pyrolysis products of [^{14}C] in cigarette smoke.

Chemical Standards:

The registrant states that they will use the following analytical standards: [S-Methyl-^{14}C]Acephate. Chemical Name: O,S-dimethyl acetylphosphoramidothioate (IUPAC) CAS No. 30560-19-1. The Non-radiolabeled chemical purity will be analytical grade. The actual purities of the non-labeled acephate and radiolabeled standards will be provided in the Final Report. The specific activity is stated to be approximately 282 μCi/mg (51.6 Ci/mM) with the actual value to be included in the Final Report as well.

Test Substance:

The amount of actual test substance needed stated by the registrant:
Non-Radiolabeled- Approximately 50 mg
Radiolabeled- Approximately 0.7mg; approximately 0.2 mCi.

The [^{14}C]acephate will be mixed with its analytical reference grade standard to obtain sufficient chemical with specific activity of approximately 20 μCi/mg. The specific activity of the labeled test compounds is approximately 282 μCi/mg. A 50 ml solution of 100 μg/ml fortifying standard solution with the desired specific activity of 20 μCi/mg will be prepared by dissolving 0.1 mCi or 0.35 mg of [^{14}C]acephate and 4.5 mg of the respective analytical reference standard in 50 ml of methanol.

Number of Samples: A minimum of three cigarettes yielding a mass balance of $\geq$90% of total tobacco radioactivity each will be smoked to establish smoke distribution.

Cigarette Preparation: University of Kentucky (2R1 or equivalent) cigarette tobacco (shredded) will be sprayed with the desired fortifying standard in methanol (using an atomizer, and limiting the volume to 0.5 ml/g of the tobacco to obtain a 50 ppm level of acephate on the tobacco. Mixing will be followed by

evaporation of the solvent and the tobacco will be conditioned at approximately 60 % RH and 75°F to obtain 16 % moisture in the tobacco. The tobacco will be rolled into cigarettes using an Export A rolling machine. Cigarettes will be equilibrated to 13% moisture for smoking. The total radioactivity present in the equilibrated cigarettes will be determined by radioassay. Subsamples of the tobacco will be taken and combusted in a sample oxidizer such as the Packard 306 oxidizer. Each cigarette will be uniquely identified by notebook reference and cigarette number, stored refrigerated in a closed container prior to use.

CBRS Response: Cigarettes should be about 70 mm long, contain approximately 1 gram of cut tobacco, and should be **unfiltered**. Total radioactive residues in randomly selected cigarettes should be determined in at least 2-3 cigarettes by liquid scintillation counting (LSC). All cigarettes should be refrigerated until required for smoking.

Total Smoke Distribution Studies: The TSRA (total recovery smoking apparatus) will be used to simulate the pyrolytic conditions found in the smoking of cigarettes made from tobacco bearing acephate residues. The smoking apparatus is designed to collect MS and SS (mainstream and sidestream smoke) for the quantitative collection of SS and MS smoke particulate residues and gases. This allows the quantitative distribution and identification of the ^{14}C containing components of the trapped smoke.

CBRS Response: Particulate matter should be trapped on glass fiber filter discs. Five cigarettes should be smoked per experiment with a minimum of five smokings performed. Cigarettes should be smoked to a standard butt length (20 mm), and the number of puffs per cigarette recorded.

Analytical Procedures: Using TLC, HPLC, and/or GC for identification of components, the gas scrubbing traps, Cambridge filters, and smoking chamber will be directly analyzed, rinsed or extracted with appropriate solvents. MS and SS (main stream and side-stream) gas phases will be trapped into separate coiled stainless steel tubes immersed in liquid nitrogen, condensed gas components purged from the trap with helium or solvent and analyzed by GC with radioactivity monitoring detector and flame ionization detection (FID). Radioactivity detection and FID will be done separately. No less than two types of chromatographic analysis will be performed for identification/characterization of ^{14}C-residues present at $\geq$10% of the total tobacco radioactivity present in extracts, rinses, or trapping media. Confirmation of identified components will be attempted by GC- or LC-mass spectrometry.

cc: RF, SF, List A Rereg. F., Tobacco Cultural Pract's F., Circ., DEH.
Disc: B:\ACEPHATE\PYROLYSI.PRO
RDI: RSQuick: 10/20/95 R. B. Perfetti: 10/24/95 EZager: 10/26/95.