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DUPONT

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

LEGAL DEPARTMENT

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June 21, 1966

Petitions Control Branch
Food and Drug Administration
Department of Health, Education, and Welfare
Washington, D. C. 20204

Attention Mr. Willard G. Orr, (3)
Food and Drug Officer

Dear Mr. Orr:

Food Additive Petition 5B1747

By letter dated January 14, 1966, we supplemented the above petition by filing Ninety-Day Feeding Studies of (b) (4) paper fluorodizer in the rat and dog. On March 22, 1966, we met with Messrs. Blumenthal, Detweiler, McLaughlin, and you to discuss whether the level of application/migration of (b) (4) could be brought into line with the levels of safety shown in the toxicity studies.

We have now determined what would be the practical, commercial use levels for the product on paper intended for oil-resistant wrapping materials. In surface applications of (b) (4) solids on 200-pound bleached sulfite container board, these levels are 0.217% and 0.267% (b) (4) on weight of paperboard. In the petition as originally filed, at page 5, it is stated that the initial extraction tests were run with 0.5% (b) (4) on weight of paper, an application level roughly double the maximum actually required for oil repellency. The application procedure was the same as that described in the petition, as originally filed. Extractions were run with distilled water at 150°F. for 0.5 hour and at 70°F. for 48 to 70 hours and, with Wesson Oil, at 100°F. for 0.5 hour.

Attached and marked "Exhibit 1" is a table showing the extraction results under the revised levels of application. There is no migration determinable for the Wesson Oil extractions or for water at 70° for 48 to 70 hours. There are average extractions of 0.1 and 0.2 ppm (b) (4) solids for water at 150° for 0.5 hour. These findings indicate that (b) (4) will find its way into food

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only in exceptional circumstances. Since (b) (4) is an oil and fat repellent, it will be used primarily to package fatty foods and there will be no detectable migration as the fats and oils are repelled. Water at high temperatures causes the most migration, but practically all moisture-bearing foods packaged in (b) (4) -treated paper and paperboard will be packaged and stored at room temperature, under which conditions there is no detectable migration.

The reduced levels of extraction — now at or under 0.2 ppm — are attributable not only to reduced levels of application, but also to a correction in the assay of total fluorine in the blank. In the original extraction studies, the valves under the column headed "total fluorine ppm blank" represented the flourine in the solvent, but did not include flourine extracted from the paperboard. Since, as we indicated in the original petition, there is an average of 120 ppm fluorine in the blank paperboard, it is to be expected that some will migrate. Thus Exhibit 1 shows increased values of total fluorine extracted from the blanks, which of course means that proportionally smaller amounts of (b) (4) will migrate than we had originally figured.

In the 90-day feeding study in rats with (b) (4) the question was raised whether the slightly enlarged, but histologically normal, livers observed in rats that received 500-1000 ppm (b) (4) for 90 days may have resulted from the diethanolamine moiety of the molecule. (b) (4) contains 16-17% diethanolamine; rats receiving the intermediate dietary level of (b) (4) (500-1000 ppm) received an average daily dose of approximately 60 mg/kg (b) (4) or 10 mg/kg diethanolamine. Smyth, Jr., et al. (Mellon Institute of Industrial Research, University of Pittsburgh, Report 13-67) have shown that 20 mg/kg/day diethanolamine for 90 days produced neither liver enlargement nor pathologic changes, but that 90 mg/kg/day did; it was stated that the no-effect level was between 20 mg/kg/day and 90 mg/kg/day. It would appear, therefore, that the slightly enlarged livers observed in the 500-1000 ppm dietary level were not attributable solely to the diethanolamine moiety, but probably to the combination of this moiety and the fluorocarbon moiety.

Considering the revised extraction data which shows that the commercially useful level of application will result 0.2 or less ppm of (b) (4) migrating into food, it is submitted that a regulation limiting (b) (4) in food to 0.2 ppm or less would be consistent with the safety data already on file.

Very truly yours,

[redacted]

Richard H. Rea

RHR:lkr

Enc.