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Nationwide Surveillance of Angiosarcoma of the Liver

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and the authors in publishing a very much needed report and hoping that you will accept in good spirit the criticisms I have directed toward the utilization of out-moded terminology that will make this report very difficult to code and properly cite in the toxicological literature where it truly belongs in an important place.

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Reply

We can only admit that the comments made by Dr. Griffith E. Quinby on the nomenclature of diphenyl vs biphenyl are well founded and true. However, the use of this nomenclature still varies, and the designation of diphenyl has not yet been abandoned by several well-known dictionaries or encyclopedias, eg, *Chamber's Technical Dictionary*, third revised edition, New York, 1965, p 247, *The Merck Index: An Encyclopedia of Chemicals and Drugs*, eighth edition, 1968, p 387, and *Encyclopaedia of Occupational Health and Safety*, volume I, A-K, pp 391-392, International Labour Office, Geneva, 1971. In all these books the word "diphenyl," alone or as main title word is used. It is astonishing that this word actually appears in the *Handbook of Analytical Toxicology* (editor, Irving Sunshine), published by the Chemical Rubber Co., 1969, in one place (p 1062) even as the main title word. This is remarkable because in the *Handbook of Chemistry & Physics* by the same publisher, only biphenyl is used, as pointed out by Dr. Quinby. Regardless of these remarks, we do agree with Dr. Quinby, and we shall from now on use only the word "biphenyl."

As to Dr. Quinby's second question, we have considered very thoroughly the possibility that some impurities of biphenyl could have contributed to toxic symptoms. We have examined the technical biphenyl used for impregnation of fruit wrapping paper, and two kinds of a laboratory reagent biphenyl (Diphenyl, made by British

Drug Houses Ltd., England and Biphenyl, purum, made by Fluka AG, Switzerland). The melting points of all these preparations and their mixtures were the same, 70.0 to 70.5 C, measured by a melting point meter. The reflective indexes of those preparations were also the same, n_D^{77} 1.586.

We also compared the infrared spectra of both substances and we did not find any difference between these substances.

We further examined the compounds gas chromatographically and found the chromatograms of both preparations qualitatively and quantitatively identical. According to the facts presented, we are convinced that the biphenyl used for the impregnation of fruit paper in our case has been a very pure compound. Thus, we do not believe that there could have been any other as yet unidentified chemical or impurity in the technical biphenyl used, responsible for poisonings. And even if this were the case, the unknown impurity must possess an extraordinarily high toxicity, at least 100 to 1,000 times that of biphenyl. It seems unlikely to imagine that such a compound is hidden in the technical biphenyl.

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Nationwide Surveillance of Angiosarcoma of the Liver

To the Editor.—The National Institute of Occupational Safety and Health and the Bureau of Epidemiology, Center for Disease Control, have recently established a surveillance registry for cases of angiosarcoma of the liver in the United States. This is in response to the recent discovery that at least some cases of this tumor may stem from exposure to vinyl chloride. Physicians who have patients with this diagnosis currently under their care or who have encountered such cases in their practice over the past ten years are urged to contact the Center for Disease Control. Information is desired concerning all such cases, regardless of assumed etiology. Address all information to: Center for Disease Control, Bldg 1, Room 520, Atlanta, GA 30333—phone (404) 633-3311, ext 3961.

Angiosarcoma of the liver is an exceedingly rare tumor. It is estimated that no more than 15 to 25 cases occur each year in the entire United States. The possible relationship of this tumor to vinyl chloride exposure was first suggested when it was realized that four such cases had been diagnosed since 1968 in workers at a single polyvinyl chloride production plant.¹ Since that time, three additional cases have been identified in workers at this plant, and single cases have been reported at two other plants.

All 4 of the initial patients had worked for at least 14 years before diagnosis in various phases of the vinyl chloride polymerization process. Each of the four showed evidence of coexisting hepatic fibrosis in the absence of heavy alcohol intake, prior hepatitis, or exposure to hepatotoxic agents outside the work environment. (In particular, there was no evidence of exposure to thorium dioxide or arsenic, two chemicals previously implicated as causes of this tumor in man.^{2,3})

Epidemiologic studies are underway to define more precisely this apparent relationship between hepatic angiosarcoma and exposure to vinyl chloride. The national surveillance registry is a vital part of this effort, both as a measure of past and present incidence in the United States, and as a means by which to gauge what proportion of cases may indeed be related to vinyl chloride. Full participation by physicians in this case surveillance effort is urgently solicited.

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