Blood Lipid Concentrations of Dioxins and Furans in a Sample of BASF Employees Included in the IARC Registry of Workers Exposed to Phenoxy Acid Herbicides and/or Chlorophenols

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Depending on process conditions, polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) may be generated as low-level byproducts of chlorophenol and chlorophenoxy herbicides manufacture. A stratified random sample of 20 active employees from a cohort of phenoxy herbicide workers was selected in 1995 for determining PCDD and PCDF concentrations in blood lipids to assess the extent of past PCDD and PCDF exposure in this cohort and whether that exposure might explain site-specific cancer findings in the total cohort. This cohort is included in the IARC International Registry of Persons Exposed to Phenoyxacid Herbicides and Their Contaminants. For the 19 persons who participated, median PCDD and PCDF concentrations were comparable to background concentrations in the general population. Median levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin, the sum of hexachlorodibenzo-p-dioxin, pentachlordibenzofurans, and two dioxin toxicity equivalents values were statistically higher in 7 employees assigned to synthesis operations than for 12 employees assigned to other operations. However, the PCDD and PCDF concentrations were low relative to those seen in other dioxin-exposed cohorts. We conclude that PCDD and PCDF exposures of cohort members are unlikely to explain the elevated standardized mortality ratios observed in this cohort for several cancer sites. — Environ Health Perspect 106(Suppl 2):733-735 (1998). http://ehpnet1.niehs.nih.gov/docs/1998/suppl/2-733-735messerer/abstract.html

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Introduction

Recently, the International Agency for Research on Cancer (IARC) established an international registry of workers potentially exposed to phenoxy herbicides and chlorophenols that incorporated data from 24 cohorts in 11 countries (1). The purpose of the registry was to further investigate possible long-term health effects associated with manufacturing or using these substances. In Germany, three companies, including BASF Aktiengesellschaft, agreed in 1987 to participate in the study. The German component of the study was coordinated by the Division of Epidemiology of the German Cancer Research Center, Heidelberg, Germany and was conducted according to a study design described by Becher et al. (2). The general exposure assessment process was detailed by Kauppinnen et al. (3) and was based on plant visits and the collection of extensive data on process descriptions, production statistics, and work conditions.

The BASF subcohort consisted of 680 male employees of German nationality with at least 1 month of employment in chlorophenoxy herbicide operations. This subcohort specifically did not include persons assigned to a trichlorophenol production facility in which a decompositon reactor accident had occurred in November 1953. [Employees involved in clean-up and other support activities after the 1953 accident who were possibly exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) have been subjects of numerous occupational health studies (3).]

A cohort mortality study of the German subcohorts (four work locations of three companies) with mortality follow-up through 1989 was recently published by Becher et al. (4). Within the BASF subcohort, there were 93 deaths of which 29 were due to cancer. Cause-specific mortality analyses within the BASF subcohort yielded an overall standardized mortality ratio (SMR) of 85 (95% confidence interval [CI] 68–104) for all causes of death and an SMR of 110 (95% CI 73–158) for all malignancies. A statistically elevated SMR was observed, however, for deaths due to cancer of the buccal cavity and pharynx (SMR 822, 95% CI 300–1789).

Evaluation of mortality experience within the entire IARC cohort including the German subcohorts is given in Kogevinas et al. (5). In a previous exposure assessment paper, Kauppinnen et al. (1) acknowledged variability in the potential for dioxin exposure across subcohorts within the IARC registry and recommended that biological monitoring be considered a way of improving the exposure assessment. Given that the preference for direct exposure measurements was practical, we selected a random sample of members of the BASF subcohort and sought their cooperation in a substudy to measure polychlorinated dibenzo-p-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) concentrations in blood lipids. Because of the long biological half-life of many PCDD and PCDF congeners (6,7), currently measured dioxin concentrations reflect cumulative dioxin exposures that may have occurred over many years. In this paper, we compare findings for the BASF subcohort with previously published data for the general population and for workers from two other German subcohorts.

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Abbreviations used: CI, confidence interval; PCDD, polychlorinated dibenzo-p-dioxins; PCDF, polychlorinated dibenzofurans; ppt, parts per trillion; SMR, standardized mortality ratio; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin; TEQ(1), international toxicity equivalents; TEQ, toxicity equivalents.
Material and Methods
A stratified random sample of 20 currently employed members of a BASF subcohort of chlorophenoxy herbicide workers was selected in 1995. Stratification was based on the type of work activity—synthesis, formulation, maintenance, and other—to allow comparison of PCDD and PCDF concentrations across different operations. Each of the 20 selected employees was sent a letter explaining the purpose of the study and asking for their written consent to provide a blood specimen for dioxin determinations. All except one employee (a synthesis worker) agreed to participate.

Blood lipid analyses were performed by ERGO-Forschungsgesellschaft (Hamburg, Germany), according to methods described previously (7). Individual results were explained in written form to all 19 participants. Regular medical examinations are offered to employees who have TCDD concentrations above 5 ppt or international TCDD toxicity equivalent (I-TEQ) values above 40 ppt. Comparisons between subgroups of employees, defined by work activity, were based on a two-sided nonparametric analysis (Wilcoxon test, RS/1, Release 4, BBN Software Products Corporation, Cambridge, MA).

Results
Summary findings for the 19 study participants overall and subdivided by prior work activity (synthesis vs other operations) are given in Table 1. In addition, German background concentrations for various PCDD and PCDF congeners determined by the same laboratory are also provided in the table. The median background values were based on data for 36 individuals (median age 53 years) reported by Päpke et al. (8). The median age in the study population was 52 years (range 35–59 years). In general, the sample medians of the BASF subgroup are comparable to or somewhat lower than the median values for the German background group. Comparisons between the synthesis subgroup and employees assigned to other activities revealed statistically increased levels of TCDD, the sum of hexa-CDD, and the sum of penta-CDF, and both TEQ values in the synthesis subgroup. The median levels in the synthesis subgroup were somewhat above German background levels. Individual distributions of I-TEQ and TCDD results for synthesis compared to all other employees are shown in Figures 1 and 2.

Table 1. Median PCDD and PCDF concentrations (ppt) in a sample of workers from BASF.

| Substance                  | Background values* | Total, n=19 | Synthesis, n=7 | Other, n=12 | p Valueb |
|----------------------------|---------------------|-------------|---------------|-------------|---------|
| 2,3,7,8-Tetra-CDD          | 3.2                 | 2.7         | 3.8           | 2.0         | 0.038   |
| 1,2,3,7,8-Penta-CDD        | 7.5                 | 6.2         | 9.9           | 5.0         | 0.066   |
| Sum hexa-CDD               | 47.8                | 42.3        | 76.0          | 38.2        | 0.048   |
| 1,2,3,4,6,7,8-Hepta-CDD    | 48.1                | 48.6        | 77.2          | 43.3        | 0.072   |
| 1,2,3,4,6,7,8,9-Octa-CDD   | 362.7               | 378.4       | 464.3         | 318.9       | 0.490   |
| 2,3,7,8-Tetra-CDF          | 1.8                 | 2.0         | 2.0           | 2.0         | —       |
| Sum penta-CDF              | 18.0                | 12.5        | 24.6          | 11.3        | 0.027   |
| Sum hexa-CDF               | 13.1                | 14.6        | 22.6          | 13.6        | 0.127   |
| Sum hepta-CDF              | 9.7                 | 9.7         | 10.0          | 9.7         | 0.881   |
| 1,2,3,4,6,7,8-Octa-CDF     | 2.5                 | 5.0         | 5.0           | 5.0         | —       |
| German TEQ (BGA/UBA)       | 14.6                | 10.5        | 21.9          | 9.7         | 0.001   |
| I-TEQ                     | 25.0                | 18.5        | 35.4          | 15.3        | 0.001   |

*According to Päpke et al. (8). bComparison between synthesis and other workers.

Discussion
Median values of various dioxin and furan congeners in this sample of employees from a BASF phenoxy herbicide subcohort were comparable to German background concentrations and were low in comparison to those observed for other dioxin-exposed cohorts. There were also no historical cases of chloracne reported within the BASF subcohort (4). The IARC registry of workers exposed to phenoxy herbicides and chlorophenols includes four different cohorts from three companies. PCDD and PCDF measurements are available for two of the other German cohorts and for several cohorts from other countries. Summary measurement data for these cohorts are presented by Kogevinas et al. (5), and data for two of the German cohorts are presented in more detail by Fleisch-Jansys et al. (9) and Jansing and Korff (10). For these latter two cohorts, median dioxin concentrations expressed in TEQ units were 141 and 402 ppt; these measurements are two orders of magnitude higher than that observed in the present subcohort. Because the time between exposure and blood measurement is comparable across all three German cohorts, varying elimination periods cannot explain these differences.

The measured values in this group of employees are only slightly above background levels even within the synthesis subgroup. It is therefore unlikely that the marginally increased SMRs for total cancer and lung cancer and the statistically increased SMR for cancer of the buccal cavity and pharynx in the BASF cohort, as described by Becher et al. (4), can be attributed to PCDD or PCDF exposure. Only one of the employees with oral cancer had worked in synthesis (4). Findings of Ott and Zober (3) are consistent with a TCDD-induced increased cancer risk, but only in persons with past exposures sufficient to cause other signs of toxicity, e.g., chloracne.
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