Carbofuran is a carbamate insecticide registered for use on a variety of food crops including corn, alfalfa, rice, and tobacco. An estimated 5 million pounds of carbofuran is used annually in the United States, and 45% of urban African-American women have detectable levels of carbofuran in their plasma. Nitrosated carbofuran has demonstrated mutagenic properties. We examined exposure to carbofuran and several tumor sites among 49,877 licensed pesticide applicators from Iowa and North Carolina enrolled in the Agricultural Health Study. We obtained information regarding years of use, frequency of use in an average year, and when use began for 22 pesticides using self-administered questionnaires. Poisson regression was used to calculate rate ratios (RR) and 95% confidence intervals (CIs) adjusting for potential confounders. Lung cancer risk was 3-fold higher for those with > 109 days of lifetime exposure to carbofuran (RR = 3.05; 95% CI, 0.94–9.87) compared with those with < 9 lifetime exposure days, with a significant dose–response trend for both days of use per year and total years of use. However, carbofuran use was not associated with lung cancer risk when nonexposed persons were used as the referent. In addition, carbofuran exposure was not associated with any other cancer site examined. Although carbamate pesticides are suspected human carcinogens, these results should be interpreted cautiously because there was no a priori hypothesis specifically linking carbofuran to lung cancer. Key words: agriculture, cancer incidence, carbofuran, lung cancer, pesticides. Environ Health Perspect 113:285–289 (2005). doi:10.1289/ehp.7451 available via http://dx.doi.org/
level of agreement for pesticide use was similar to other factors routinely estimated with epidemiologic questionnaires (Blair et al. 2002).

For these analyses, we estimated exposure with total lifetime exposure-days to carbofuran. Lifetime exposure-days was defined as the product of the number of years a participant personally mixed or applied carbofuran and the number of days in an average year that carbofuran was used. In addition, we incorporated an algorithm developed by Dosemeci et al. (2002) to estimate an exposure intensity score and applied it to lifetime exposure-days metric. Briefly, the intensity score was designed to incorporate aspects of pesticide use that can modify actual exposure, including whether an applicator personally mixed or prepared the pesticides for application, what type of application methods were used, the repair of pesticide application equipment, and the use of personal protective equipment during these activities. Dermal absorption is generally considered the major route of exposure for pesticide applicators (Maroni et al. 2000; Tobin 1970). Therefore, the intensity score heavily weighted the use of protective gloves and to a lesser extent protective clothing. We calculated intensity-weighted exposure-days as the product of the intensity score and total lifetime exposure-days. In addition to these exposure metrics, we also assessed the frequency (i.e., number of days/year applied) and the duration (total number of years applied) of carbofuran exposure in relation to cancer risk.

Statistical analysis. Prevalent cancer cases (n = 1,074) and applicators who failed to provide information about carbofuran use (n = 6,360) were excluded, leaving 49,877 cohort members from this analysis. Most of the subjects who were missing information on carbofuran use and other potential confounders were from North Carolina (64%). Two reference groups were used for these analyses: pesticide applicators who reported never using carbofuran and pesticide applicators whose use of carbofuran was in the lowest tertile of exposure. We used Poisson regression to calculate rate ratios (RR) and 95% CIs. Lifetime exposure-days and intensity-weighted lifetime exposure-days to carbofuran were categorized into tertiles based on the distribution in all the cancer cases. The highest tertile was then divided at its midpoint to increase the resolution at higher exposure levels. We limited analyses to tumour sites where there were more than five cases in each category of exposure. Models were adjusted for age at enrollment (< 40, 40–49, 50–59, ≥ 60 years), sex, education (≤ high school graduate, > high school graduate), smoking (by pack-years: never, ≤ 14, > 14), alcohol consumption during the last 12 months (yes/no), family history of cancer (yes/no), year at enrollment, state of residence (Iowa/North Carolina), and the five pesticides most highly correlated with carbofuran use [permethrin (crop), S-ethyl dipropylthiocarbamate (EPTC), chlorpyrifos, fonofos, and trichlorfon: never, low, high exposure]. The correlation coefficients for these five pesticides ranged between 0.69 (permethrin) and 0.85 (trichlorfon). The cut point that dichotomized low and high exposure for each pesticide correlated with carbofuran was determined by the median for lifetime exposure-days for that particular pesticide. We based the cut points for days of use per year and years of use on the categorical responses to the following questions: “In an average year when you personally used this pesticide, how many days did you use it?” (< 5 days; 5–9 days; 10–19 days; 20–39 days; 40–59 days; 60–150 days; or > 150 days) and “How many years did you personally mix or apply this pesticide?” (≤ 1 year or less; 2–5 years; 6–10 years; 11–20 years; 21–30 years; or > 30 years). For the analysis, we collapsed the upper categories to ensure that there were approximately five or more cases in each category. We determined the most parsimonious model (reduced) with −2 log-likelihood ratio tests by removing each covariate from the saturated (full) model and retaining only those variables that resulted in significant −2 log-likelihood ratio (Hosmer and Lemeshow 1989). The most parsimonious model included age, smoking (never, < 14 pack-years, and ≥ 14 pack-years of smoking), family history of cancer, and trichlorofon and permethrin exposure.

To further control for potential confounding by smoking, we also adjusted for several other smoking variables including smoking status (never, former, current), pack-years of smoking, duration of smoking, and number of cigarettes smoked per day. The inclusion of these additional smoking variables did not appreciably alter the risk estimates and were not retained in the models. Linear trends were assessed using the p-value of the coefficient of the exposure treated as a continuous variable using the median value for each tertile of exposure in the models also adjusting for covariates (Breslow and Day 1987). Tests for interaction were performed by determining the significance of the coefficient of the product term of the exposure and the purported effect modifier.

Table 1. Selected characteristics of applicators, by carbofuran exposure (no. [%]) in the AHS (1993–1997).

| Characteristic | Nonexposed | Low exposed | High exposed |
|---------------|------------|-------------|--------------|
| Age (years)   |            |             |              |
| < 40          | 14,023 (37.6) | 1,032 (21.8) | 1,729 (22.1) |
| 40–49         | 10,217 (27.4) | 1,470 (31.0) | 2,532 (32.1) |
| 50–59         | 6,802 (18.3)  | 1,216 (25.7) | 2,056 (26.1) |
| ≥ 60          | 6,210 (16.7)  | 1,016 (21.5) | 1,557 (19.7) |
| Sex           |            |             |              |
| Male          | 36,069 (96.8) | 4,698 (99.2) | 7,819 (99.2) |
| Female        | 1,190 (3.2)  | 36 (0.8)    | 65 (0.8)     |
| State         |            |             |              |
| Iowa          | 25,459 (68.3) | 3,421 (72.3) | 4,908 (62.3) |
| North Carolina| 11,800 (31.7) | 1,313 (27.7) | 2,976 (37.7) |
| Applicator type|            |             |              |
| Farmer        | 33,341 (89.5) | 4,574 (96.6) | 7,355 (83.3) |
| Commercial    | 2,918 (10.5)  | 180 (3.4)   | 529 (6.7)    |
| Smoking       |            |             |              |
| Never         | 19,976 (54.0) | 2,509 (53.2) | 4,056 (51.6) |
| Former        | 10,587 (28.7) | 1,577 (33.4) | 2,560 (32.6) |
| Current       | 6,396 (17.3)  | 635 (13.5)  | 1,241 (15.8) |
| Alcohol use*  |            |             |              |
| Yes           | 25,352 (69.0) | 3,260 (69.1) | 5,290 (67.8) |
| Education     |            |             |              |
| ≤ High school | 21,270 (57.2) | 2,503 (53.0) | 4,372 (55.5) |
| > High school | 15,897 (42.8) | 2,219 (47.0) | 3,504 (44.5) |
| Family history of cancer | | | |
| Yes           | 13,339 (38.0) | 2,099 (46.5) | 3,404 (45.9) |
| Corn production|            |             |              |
| Yes           | 24,967 (67.0) | 3,801 (80.0) | 6,226 (79.0) |
| Other pesticide use | | | |
| Trichlorofon  | 305 (0.8)   | 37 (0.8)    | 160 (2.1)    |
| Fonofos       | 5,410 (14.5) | 1,591 (34.4) | 2,969 (38.8) |
| Chlorpyrifos  | 12,908 (34.7) | 2,534 (53.8) | 4,382 (63.5) |
| EPTC          | 6,112 (16.8)  | 1,351 (29.5) | 2,417 (31.8) |
| Permethrin#   | 4,076 (11.1)  | 813 (19.9)  | 2,063 (27.1) |
| Person-years  | 240,649.2    | 298,679.9   | 508,522.7    |
| No. of other pesticides used# | 11.5 ± 6.6 | 18.3 ± 6.6 | 20.4 ± 7.2 |
| Follow-up (years)# | 6.5 ± 1.4 | 6.3 ± 1.4 | 6.5 ± 1.4 |
| Smoking (pack-years)# | | | |
| Former smokers| 15.4 ± 20.1  | 15.0 ± 18.9 | 15.8 ± 20.2 |
| Current smokers| 22.0 ± 19.9 | 24.9 ± 21.3 | 27.0 ± 22.2 |

*Reported alcohol consumption within the last 12 months. #Permethrin for use on crops. *Mean ± SD.
Results
Twenty-five percent of the pesticide applicators reported ever using carbofuran. Demographic characteristics of the non-carbofuran exposed and carbofuran exposed [categorized as low (tertile 1) and high exposure (tertiles 2 and 3)] are depicted in Table 1. The non-carbofuran exposed tended to be younger than either the low- or high-exposed carbofuran cohorts. The nonexposed were also more likely to be female than the exposed, although there were few women applicators in the study overall. Smoking status (never, former, or current), alcohol consumption in the last 12 months, attained education, state of residence, years of follow-up, and family history of cancer were all similar between the three groups. The mean number of smoking pack-years; however, sequentially increased between nonexposed, low-exposed, and the high-exposed groups. Cohort members exposed to carbofuran were more likely than nonexposed cohort members to be involved in corn production. Additionally, those exposed to carbofuran used more types of pesticides than non-carbofuran–exposed subjects.

We report on all cancer sites combined and tumor sites where sufficient numbers (at least five cases per cell) of cases occurred during follow-up to warrant statistical analyses: all lymphatic–hematopoietic cancers (Hodgkin, non-Hodgkin, multiple myeloma, and leukemia), NHL, and colon, lung, and prostate cancers.

Carbofuran exposure was not associated with the incidence of all cancers combined (Table 2) or with any tumor site examined except lung cancer. Lung cancer risk appeared to be positively associated with exposure to carbofuran when the low exposed were used as the reference group, although a test of the linear trend was not significant (p for trend = 0.07). The lung cancer rate ratio was increased 3-fold among those with more than 109 lifetime-days of use (RR = 3.05; 95% CI, 0.94–9.87). When the nonexposed were used as the reference group, however, exposure to carbofuran was not associated with the lung cancer rate ratio.

An exposure–response relationship with the intensity-weighted lifetime exposure–days was not clearly evident for lung cancer (Table 3). Although the upper category of the intensity-weighted lifetime exposure–days suggests an increase in the relative risk, the exposure–response gradient was not monotonic. Regarding the other cancer sites examined, there was no evidence of an association with intensity-weighted lifetime exposure–days when either the nonexposed or the low-exposed subjects were used as the referent (data not shown).

The risk of lung cancer also increased when the frequency of exposure (number of days of carbofuran use/year) and duration of exposure (number of years carbofuran was used) were examined separately (Table 3). However, the risk was only elevated in applicators who used carbofuran for > 10 years and for > 10 applications per year.

To further examine and characterize the association between carbofuran exposure and lung cancer, we stratified by smoking status (never, former, and current), state of residence (Iowa and North Carolina), histology (adenocarcinoma and non-adenocarcinoma), and applicator type (farmer and commercial). The analyses stratified by smoking status were limited in that only one case of lung cancer was identified among never smokers and precluded an analysis restricted to never smokers. The risk estimates increased as exposure increased for both former and current smokers (Table 4), and the p for interaction was not significant (p = 0.36). Carbofuran exposure was associated with nonsignificant increases in risk in both Iowa (2nd tertile: RR = 3.79, 95% CI, 0.73–19.55; 3rd tertile: RR = 5.90, 95% CI, 1.25–27.81) and North Carolina (2nd tertile: RR = 0.91, 95% CI, 0.41–3.74; 3rd tertile: RR = 7.87, 95% CI, 0.77–8.14). Although the point estimates of risk were greater in Iowa, the p-value for the interaction between state and carbofuran exposure was not significant (p for interaction = 0.53). Rate ratios were increased for both adenocarcinoma (2nd tertile: RR = 3.95, 95% CI, 0.41–38.02; 3rd tertile: RR = 7.87, 95% CI, 0.94–65.62) and non-adenocarcinoma (2nd tertile: RR = 1.35, 95% CI, 0.39–4.68; 3rd tertile: RR = 2.90, 95% CI, 1.0–8.36). Although the risk was considerably higher for adenocarcinoma, the p for interaction between histology and carbofuran use was not significant (p = 0.32). There was no evidence that applicator type either confounded or modified the association between carbofuran and lung cancer risk, although the number

### Table 2. RRs for selected cancers, by lifetime exposure–days to carbofuran among AHS (1993–1997) applicators with nonexposed and low-exposed groups as referents.

| Lifetime exposure days | Cases (n) | Nonexposed referent RR (95% CI) | Low-exposed referent RR (95% CI) |
|------------------------|----------|---------------------------------|---------------------------------|
| All cancers            |          |                                 |                                 |
| 0                      | 1,012    | 1.0                             |                                 |
| > 0–9                  | 151      | 0.95 (0.80–1.14)                | 1.0                             |
| 10–39                  | 115      | 0.95 (0.78–1.15)                | 1.00 (0.78–1.27)                |
| 40–109                 | 80       | 1.05 (0.83–1.33)                | 1.11 (0.83–1.49)                |
| > 100                  | 51       | 0.94 (0.70–1.26)                | 0.96 (0.67–1.37)                |
| Trendb                 |          | 0.79                            | 0.94                            |
| Lymphatic–hematopoietic cancers |     |                                 |                                 |
| 0                      | 103      | 1.0                             |                                 |
| > 0–9                  | 11       | 0.68 (0.36–1.30)                | 1.0                             |
| 10–39                  | 10       | 0.82 (0.42–1.60)                | 1.05 (0.44–2.51)                |
| 40–109                 | 11       | 1.38 (0.72–2.65)                | 1.56 (0.62–3.92)                |
| > 100                  | 5        | 0.86 (0.34–2.23)                | 0.77 (0.23–2.57)                |
| Trendb                 |          | 0.93                            | 0.74                            |
| Non-Hodgkin lymphoma   |          |                                 |                                 |
| 0                      | 44       | 1.0                             |                                 |
| > 0–9                  | 6        | 0.77 (0.31–1.86)                | 1.0                             |
| 10–39                  | 7        | 1.27 (0.55–2.91)                | 1.33 (0.44–4.02)                |
| 40–109                 | 7        | 1.40 (0.59–3.30)                | 1.09 (0.31–3.74)                |
| Trendb                 |          | 0.40                            | 0.94                            |
| Colon                  |          |                                 |                                 |
| 0                      | 80       | 1.0                             |                                 |
| > 0–9                  | 10       | 0.88 (0.45–1.72)                | 1.0                             |
| 10–39                  | 9        | 0.99 (0.49–2.02)                | 1.03 (0.41–2.56)                |
| 40–109                 | 5        | 0.84 (0.33–2.12)                | 0.77 (0.25–2.42)                |
| > 100                  | 6        | 1.34 (0.54–3.31)                | 1.16 (0.36–3.71)                |
| Trendb                 |          | 0.68                            | 0.85                            |
| Lung                   |          |                                 |                                 |
| 0                      | 98       | 1.0                             |                                 |
| > 0–9                  | 6        | 0.42 (0.18–0.97)                | 1.0                             |
| 10–39                  | 8        | 0.68 (0.33–1.43)                | 1.61 (0.55–4.69)                |
| 40–109                 | 9        | 1.09 (0.54–2.22)                | 2.54 (0.85–7.67)                |
| > 100                  | 8        | 1.38 (0.63–2.99)                | 3.05 (0.94–9.87)                |
| Trendb                 |          | 0.46                            | 0.07                            |
| Prostate               |          |                                 |                                 |
| 0                      | 372      | 1.0                             |                                 |
| > 0–9                  | 85       | 1.30 (1.01–1.66)                | 1.0                             |
| 10–39                  | 48       | 0.99 (0.73–1.35)                | 0.79 (0.55–1.13)                |
| 40–109                 | 29       | 1.03 (0.70–1.53)                | 0.86 (0.55–1.36)                |
| > 100                  | 17       | 0.88 (0.53–1.47)                | 0.73 (0.41–1.31)                |
| Trendb                 |          | 0.70                            | 0.34                            |

Rate ratios adjusted for age, sex, education, family history of cancer, smoking, alcohol, year of enrollment, state of residence, and exposure to EPTC, fonofos, trichlorofon, chlorpyrifos, and permethrin.

*Years of use > days of use per year. *p-Value for trend test.
of commercial applicator lung cancer cases was low.

Discussion

An association between carbofuran and lung cancer has not been previously reported. Several studies, however, have found pesticides (Brownson et al. 1993; Wesseling et al. 1999) and more specifically carbamate pesticides (Pesatori et al. 1994) to be associated with lung cancer, although not all studies have reported this association (McDuffie et al. 1990). In our study, lung cancer was associated with lifetime exposure-days where risk increased across exposure categories to more than a 3-fold increase in the RR in the highest category when compared with those who had applied < 9 lifetime exposure-days. The risk estimates were also elevated when the components of the lifetime exposure-days exposure metric were considered separately. Lung cancer risk, however, was not associated with carbofuran exposure when the intensity-weighted exposure-days metric was used or when non-carbofuran-exposed pesticide applicators were used as the referent.

This inconsistency between the lung cancer risk estimates when nonexposed subjects were used as the referent may be caused partly by differences between nonexposed and low-exposed groups with regard to unknown factors. Initial descriptive analyses indicated that the nonexposed and the low-exposed groups had substantial differences with regard to corn production and the total number of pesticides used. The observed differences between those with carbofuran exposure and those without carbofuran exposure raise the possibility of confounding due to other unmeasured differences between the groups. Given these differences, the low-exposed subjects may be a more appropriate reference group, although the low-exposed group may be biased as well. In addition, the inconsistency observed between the lifetime exposure-days and intensity-weighted lifetime exposure-days metrics may have occurred because the AHS intensity-weighted algorithm greatly weights dermal exposure, and this route may be less appropriate for sites where the respiratory tract is the predominant exposure route, such as the lung. Further, the intensity-weighted algorithm, as constructed, also reflects more recent use of personal protective equipment and application methods. Malignant neoplasms generally have a long latency period.

To the extent that recent exposure intensity does not accurately reflect past activities, the algorithm may increase exposure misclassification rather than reduce it.

The association between lung cancer and carbofuran exposure that we observed when the low-exposed group was used as the referent is unlikely to be confounded by smoking because pack-years of smoking was not correlated with lifetime exposure-days ($r = 0.03$) or intensity-weighted lifetime exposure-days ($r = 0.02$). Furthermore, we adjusted for smoking (never, < 14 pack-years, and ≥ 14 pack-years) in the models. Even when we used pack-years as a continuous variable or a combination of smoking status (never, former, current), number of cigarettes smoked per day and number of years smoked, the risk estimates were similar with each respective model. We also stratified by smoking status and found that the association was relatively consistent between former and current smokers. There were too few lung cancer cases to determine whether carbofuran was associated with lung cancer independent of smoking. Therefore, we cannot rule out the possibility that the association between carbofuran and the risk of lung cancer is limited to smokers and former smokers.

Agricultural exposure to endotoxin from rearing livestock has been hypothesized to reduce the risk of lung cancer (Lange et al. 2003a, 2003b, 2003c; Mastrangelo et al. 1996). Although we did not formally assess exposure to endotoxin, we conducted an analysis stratifying the cohort into those who were engaged in animal husbandry and those who were not. There was no indication that animal husbandry modified the effect of carbofuran use on lung cancer risk. In addition, engaging in animal husbandry did not confound the association between carbofuran use and lung cancer because the RRs were not altered when we included a binary animal husbandry variable in the model.

Several previous investigations of NHL have observed increases in risk associated with carbofuran exposure (McDuffie et al. 2001; Zheng et al. 2001). In addition, results from several animal models support the hypothesis that exposure to carbofuran could be a risk factor for NHL (Borzsonyi and Pinter 1977; Borzsonyi et al. 2001). In addition, results from several animal models support the hypothesis that exposure to carbofuran could be a risk factor for NHL. We found little evidence to support an association between NHL and carbofuran exposure, although relatively few cases of NHL had accrued at the time of this analysis.

There is evidence that carcinogenic $N$-nitrosocarbofuran is formed from carbofuran and nitrates in the stomach. A priori, we expected carbofuran exposure to be associated with increased risk for stomach cancer; however, at the time these analyses were conducted, too few cases of stomach cancer had occurred in the carbofuran exposed cohorts for meaningful analysis.

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Table 3. RR for lung cancer by carbofuran intensity-weighted lifetime exposure days, exposure frequency (days per year), and exposure duration (years of use) in the AHS (1993–1997).

| Intensity-weighted lifetime exposure days | Cases (n) | RR (95% CI) | p-value for trend test |
|------------------------------------------|----------|-------------|------------------------|
| > 0–63                                   | 6        | 1.0         | 1.0                    |
| 64–196                                   | 11       | 2.11 (0.77–5.78) | 2.42 (0.89–6.54)       |
| 197–487                                  | 5        | 1.19 (0.35–4.03) | 1.58 (0.48–5.19)       |
| > 487                                    | 9        | 2.10 (0.69–6.39) | 3.40 (1.21–9.58)       |
| Trend                                    |          | 0.40        | 0.23                   |

Table 4. RR for lung cancer and lifetime exposure-days to carbofuran, by smoking status in the AHS (1993–1997).

| Lifetime exposure days | Former smokers | Current smokers |
|------------------------|----------------|-----------------|
| > 0–9                  | 3              | 1.0             |
| 10–39                  | 3              | 1.87 (0.42–8.37) | 1.75 (0.39–7.90) |
| > 39                   | 11             | 4.88 (1.36–17.52) | 2.49 (0.62–10.00) |
| Trend                  |                | < 0.01          | 0.23                   |

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*Rate ratios adjusted for age, sex, education, family history of cancer, smoking, alcohol, year of enrollment, state of residence, and exposure to EPTC, fonofos, trichlorfon, chlorpyrifos, and permethrin. Rate ratios adjusted for age, smoking (never, < 14 pack-years, ≥ 14 pack-years), family history of cancer, and exposure to trichlorfon and permethrin. Rate ratios of exposure × days of use per year × intensity score. *p-Value for trend test.
There are some important limitations of this study. Although the incidence of cancers will increase as the cohort ages, currently we remain constrained by small numbers of cases for many tumor sites. For instance, only five cases of stomach cancer with exposure to carbofuran were available for analysis. The resulting statistical imprecision makes interpretation of risk estimates difficult in some instances. Another potential concern in prospective studies is loss to follow-up. However, losses to follow-up (<2%) were few and were unlikely to substantially bias the risk estimates. In addition, pesticides are commonly used as formulations where only a percentage of the total product applied is the active ingredient. Given that pesticides are applied as complex mixtures or solutions, we cannot rule out the possibility that the combination or the “inert” ingredients are the actual carcinogenic compound(s).

The strengths of this study include the prospective design, where exposure to pesticides was determined before the onset of disease, thereby eliminating the potential for recall bias. In addition, the exposure metrics used in this study represent a major improvement in the classification of pesticide exposure over previous studies, although, undoubtedly, some exposure misclassification is present in our estimates as well.

Multicolinearity between pesticides used may be another potential limitation of this study. We assessed exposure to 50 pesticides in registered pesticide applicators who, on average, used numerous pesticides. Because it is possible that carbofuran use is related to several other pesticides, we identified the five most correlated pesticides and adjusted for them in the model. Overall, exposure to other individual pesticides was highly correlated with carbofuran exposure. The correlation coefficients ranged between 0.69 (permethrin) and 0.85 (trichlorfon). However, these pesticides did not confound the association between carbofuran and lung cancer because the risk estimates were not altered when they were removed from the model. In addition, we also adjusted for cumulative lifetime application days of all pesticides, which did not appreciably alter the risk estimates.

Overall, we examined the risk of several cancer sites in relation to the carbofuran exposure. Carbofuran is a carbamate insecticide with questionable carcinogenic properties in animals. The parent compound does not seem to be genotoxic. However, the metabolites of carbofuran may be mutagenic, and there is good evidence that nitrosated carbofuran is mutagenic. This study suggests that carbofuran may be associated with an increase in the incidence of lung cancer. Conversely, carbofuran exposure was not associated with other tumor sites investigated. The results for lung cancer are provocative but should be interpreted cautiously in light of the paucity of other studies to corroborate these findings, and a reevaluation of carbofuran in the AHS cohort once more cancer cases have accrued is warranted.

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