May 25, 2012

Dr. Ruth Lunn, Director
Office of the ROC
DNTP, NIEHS
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RE: Current epidemiology study of carbon black workers

Dear Dr. Lunn,

As Chair of the Scientific Advisory Group (SAG) of the International Carbon Black Association (ICBA), I would like to respond to the NTP's request for additional information regarding an ongoing epidemiology study, results from which will be of value in the assessment of carbon black for the Report on Carcinogens (RoC). I have previously communicated with you regarding carbon black in a letter of February 27, 2012.

Background

At the most recent evaluation of carbon black by the International Agency for Research on Cancer (IARC) in 2006, the results of a USA mortality study of workers were reviewed. (Dell et al, 2006) In this cohort of over 5000 carbon black workers, no increase in overall cancer or respiratory cancer was noted. Overall cancer Standardized Mortality Ratio (SMR) was 0.83 (95% CI: 0.74-0.92), based on 330 cases. The respiratory cancer SMR was 0.87 (95% CI: 0.73-1.03) based on 129 cases.

The IARC working group, however, suggested that further analysis of the cohort include a dose response assessment, despite the fact that no overall increase in cancer or respiratory cancer was noted. The ICBA, under guidance from its SAG, invited a proposal from the authors of the USA mortality study to update the cohort and conduct a dose response assessment. (Dell et al, 2006) A proposal from Environ, with Kenneth Mundt, PhD Linda Dell, MS as co- investigators, was accepted and funded by the ICBA.

Current Epidemiology Study

The original epidemiology study was expanded to include a dose response assessment and an updated vital status determination. The study has been designed to include three phases:

Phase 1. Assess the level, quality and availability of occupational exposure data, both quantitative and qualitative (i.e. years in the industry, carbon black production process, etc). Efforts were also taken to determine the value and suitability of merging exposure data from a USA morbidity study of carbon black workers. (Harber et al, 2003) This phase has been completed.

Phase 2. Exposure reconstruction was performed by developing a cumulative exposure metric for all cohort members. (Expressed as mg/m^3-years.) This phase will be completed shortly.

Phase 3. Update mortality assessment. The 2006 study followed the cohort through 2003. This update follows the cohort through 2010, adding more power to the study. The SMR analyses will be completed by the fall of this year.

Current timetable as described by the investigators is as follows:

The exposure reconstruction will be largely completed by June 2012, with the SMR analyses completed later in the Fall 2012. Cohort names have recently been submitted to the NDI. The mortality data will then be analyzed in light of the cumulative exposure assessment.

A draft report will be prepared that summarizes all of the efforts conducted over the past few years in the study. A manuscript suitable for a peer-reviewed publication will be developed thereafter. As you know, there is considerable uncertainty in predicting the time involved in the peer review process.. Despite the time uncertainties in the peer process, it seems reasonable to expect a report acceptable for publication by mid to late 2013.

Advantages of the USA Mortality Study Update

The updated USA mortality study offers a number of advantages over the other two carbon black cohorts (UK and Germany), in which mortality risks have been evaluated. These advantages include:

- It is the world's largest carbon black cohort, with over 5000 study participants, in the mortality study. The number of workers in the dose response assessment, however, will be smaller since some cohort members lack job duty information.. In contrast to the current USA mortality study, the UK cohort consisted of 1147 workers; the German cohort consisted of 1535 carbon black workers. The USA cohort size is larger than the combined UK and German cohorts.
- Multiple plant sites will be evaluated including those actively involved in the production of carbon black. (In the UK study 5 plants were evaluated; none are currently operating. In the German study, one plant was evaluated; due to data protection laws in Germany, no further follow up of the German mortality study is possible.)
- Earlier periods of production and with apparent higher levels of exposure can be evaluated in the USA study because some cohort members date their start of employment to the 1930s.
- The study has a lengthy period of follow up (upwards of 60-70 years for some cohort members) following onset of employment. Thus, longer periods of latency can be assessed for some cohort members.
- Extensive quantitative exposure data are available, back to 1979 and conducted at periodic intervals (approximately every 3 years or so) since that time. Airborne concentrations of carbon black have been measured in the total, inhalable and respirable fractions. The availability of these quantitative exposure data allows for a more precise dose response assessment.
- The availability of the measured exposure data also allows for further testing of the "lugging" hypotheses introduced as part of an evaluation of the UK carbon black worker cohort (Sorahan et al, 2007) but not confirmed in a similar evaluation of the German carbon black worker cohort. (Morfeld et al, 2009)
- This study, like all other cohort mortality studies does not have smoking data on all cohort members. Some smoking data, however, are available from recent periodic medical examinations of workers. These data may be of value if a nested case- control study is later determined to be of value based on the results of the SMR analysis.

Summary

The USA cohort mortality study of carbon black workers will provide valuable information for the assessment of the potential risk of carbon black as a human carcinogen. The study is in the third and final phase of an effort that has been underway for over three years. Results are expected within the next year at the latest and possibly sooner.

In the event you consider a delay appropriate, I would be willing to regularly apprise you of the study's progress towards its completion.

Sincerely,

Robert J. McCunney, MD, MPH
Chair, Scientific advisory Group
International Carbon Black Association

REFERENCES

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